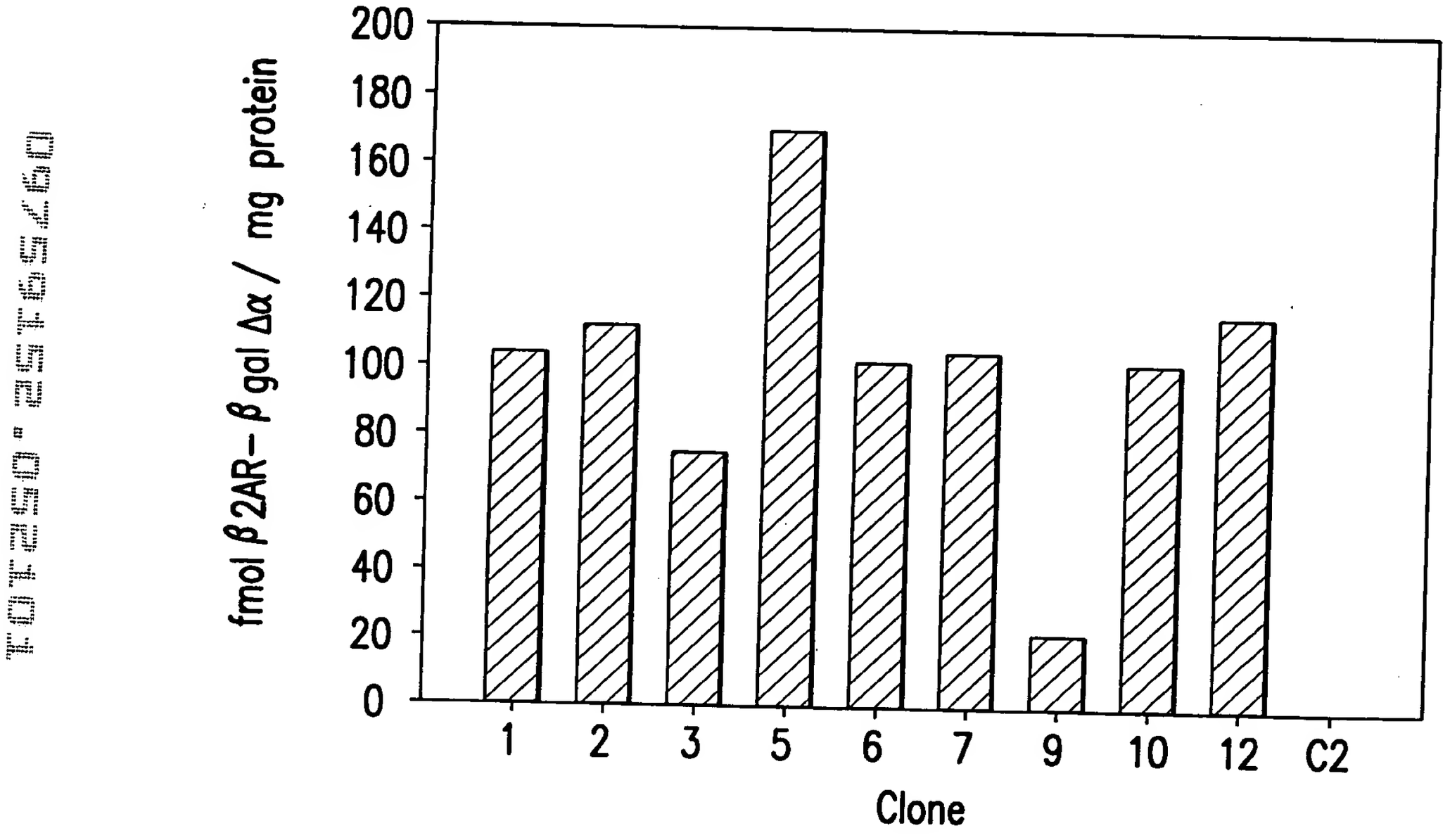

Cellular Expression of β_2AR–βgal $\Delta\alpha$ Fusion Protein in C2 Clones
(measured by anti–β–gal ELISA)
fmol β2AR–βgal $\Delta\alpha$ / mg protein
200
180
160
140
120
100
80
60
40
20
0
1
2
3
5
6
7
9
10
12
C2
Clone

FIG. 1A

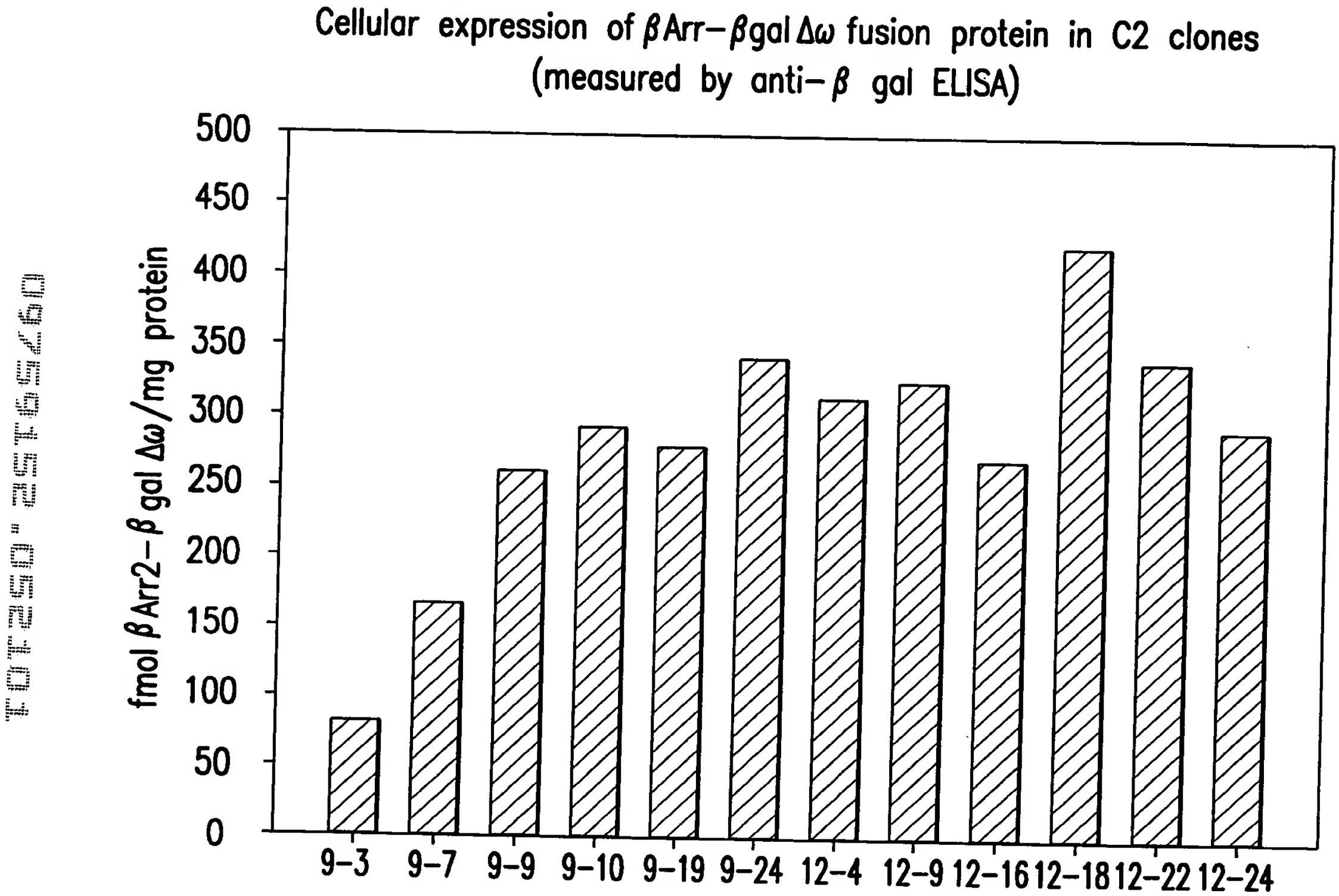

Cellular expression of βArr−βgal Δω fusion protein in C2 clones
(measured by anti−β gal ELISA)
fmol βArr2−β gal Δω/mg protein
500
450
400
350
300
250
200
150
100
50
0
9−3
9−7
9−9
9−10
9−19
9−24
12−4
12−9
12−16
12−18
12−22
12−24

FIG. 1B

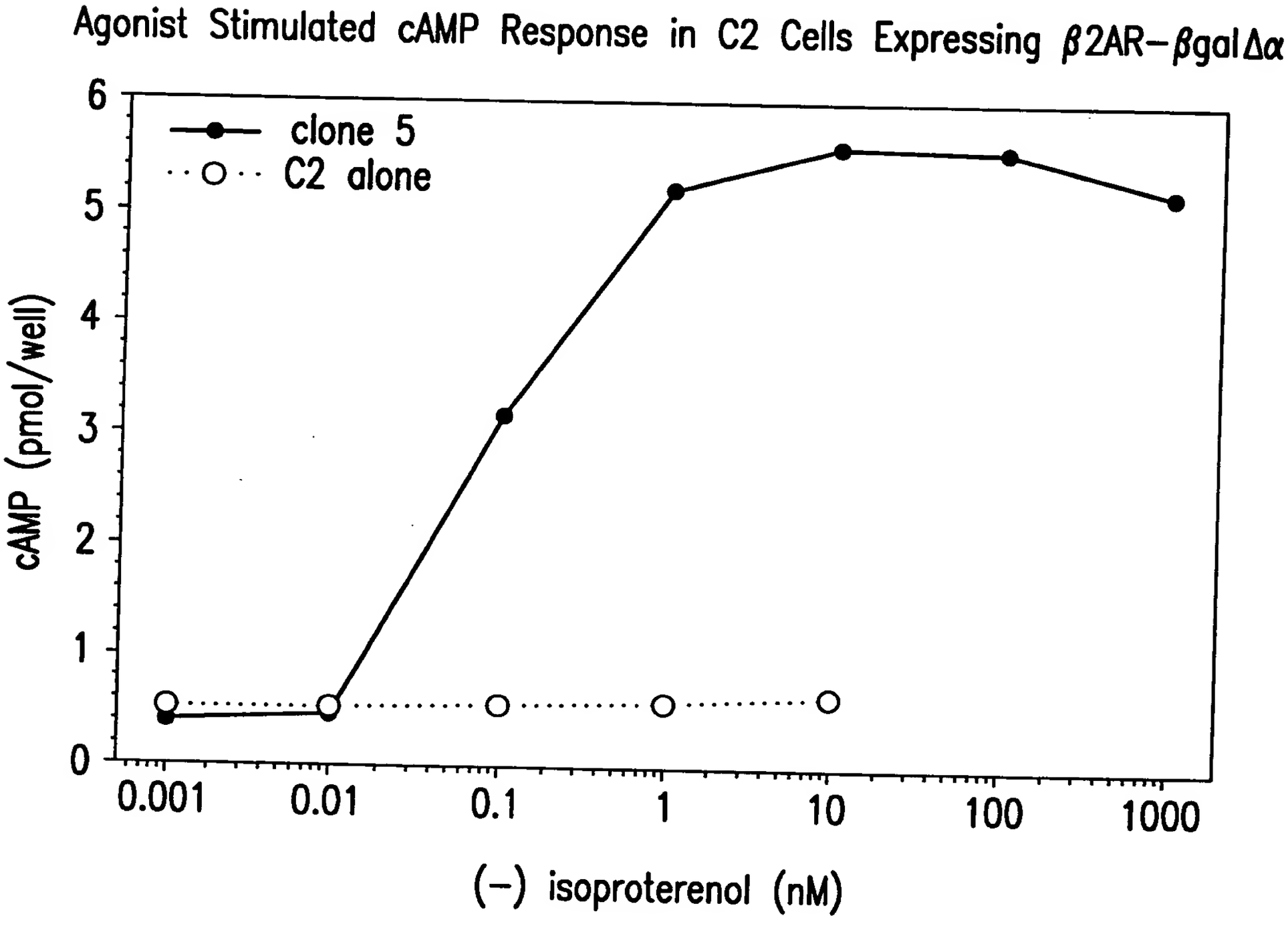

Agonist Stimulated cAMP Response in C2 Cells Expressing β2AR–βgalΔα
clone 5
C2 alone
cAMP (pmol/well)
0
1
2
3
4
5
6
0.001
0.01
0.1
1
10
100
1000
(–) isoproterenol (nM)

FIG.2

β-galactosidase Complementation as a Measurement for β_2AR-βgal Δα interacting with β Arrestin2-β gal Δω upon agonist Stimulation

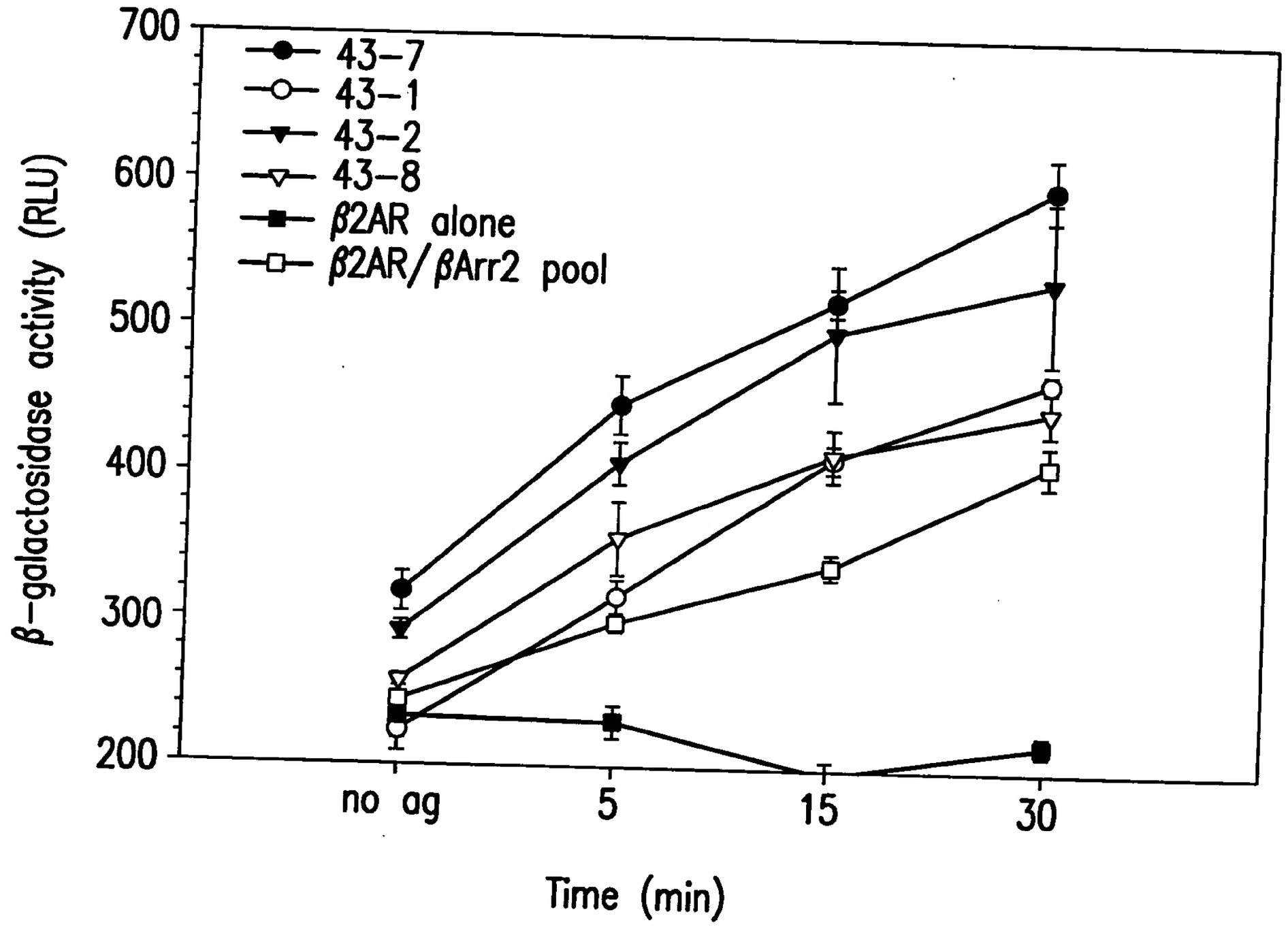


FIG. 3A

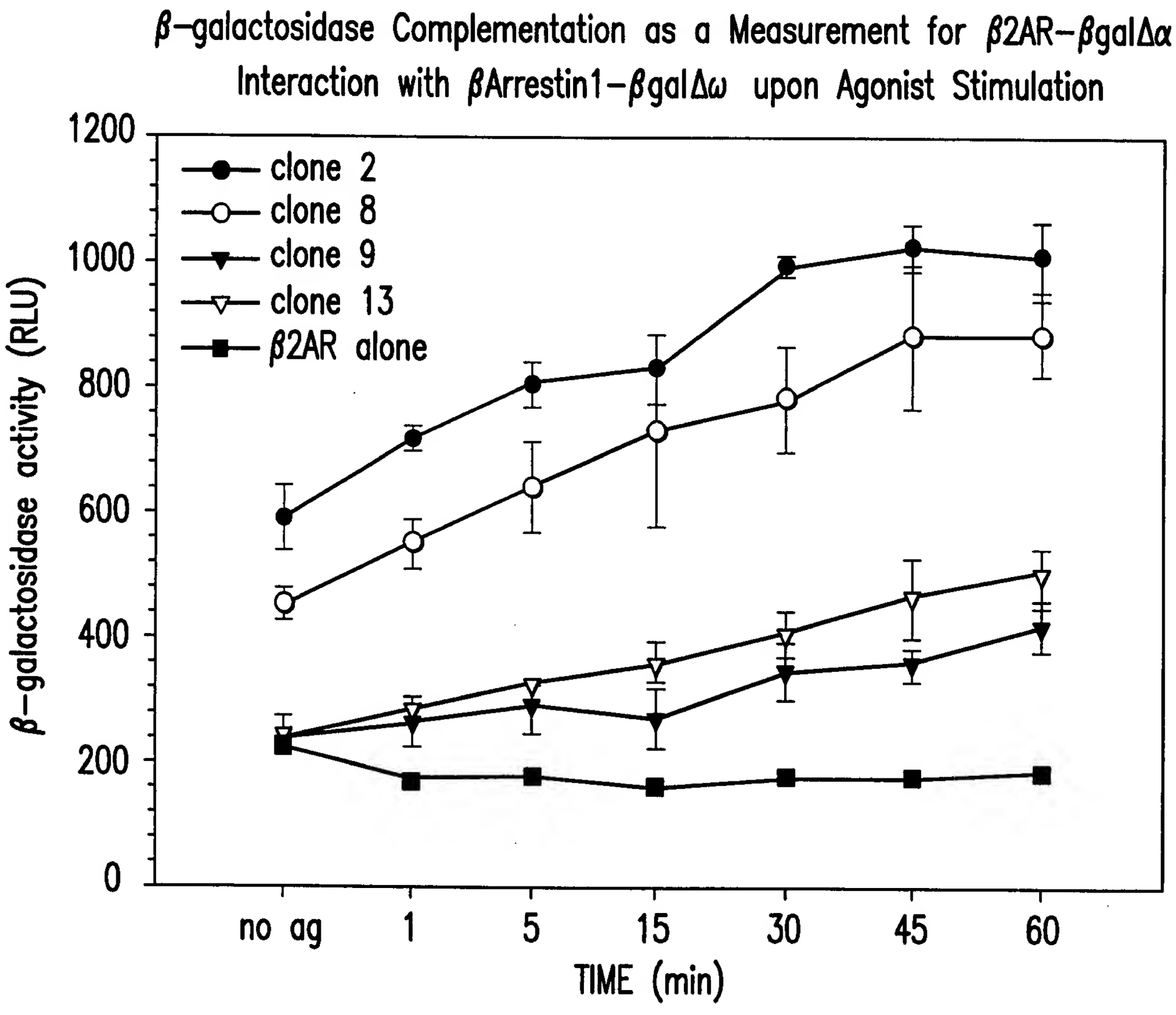

β-galactosidase Complementation as a Measurement for β2AR-βgalΔα
Interaction with βArrestin1-βgalΔω upon Agonist Stimulation
clone 2
clone 8
clone 9
clone 13
β2AR alone
β-galactosidase activity (RLU)
1200
1000
800
600
400
200
0
no ag
1
5
15
30
45
60
TIME (min)

FIG. 3B

β-galactosidase Activity in Response to Agonist in C2 Cells
Coexpressing β2AR-βgalΔα and βArrestin2-βgalΔω Fusion Proteins

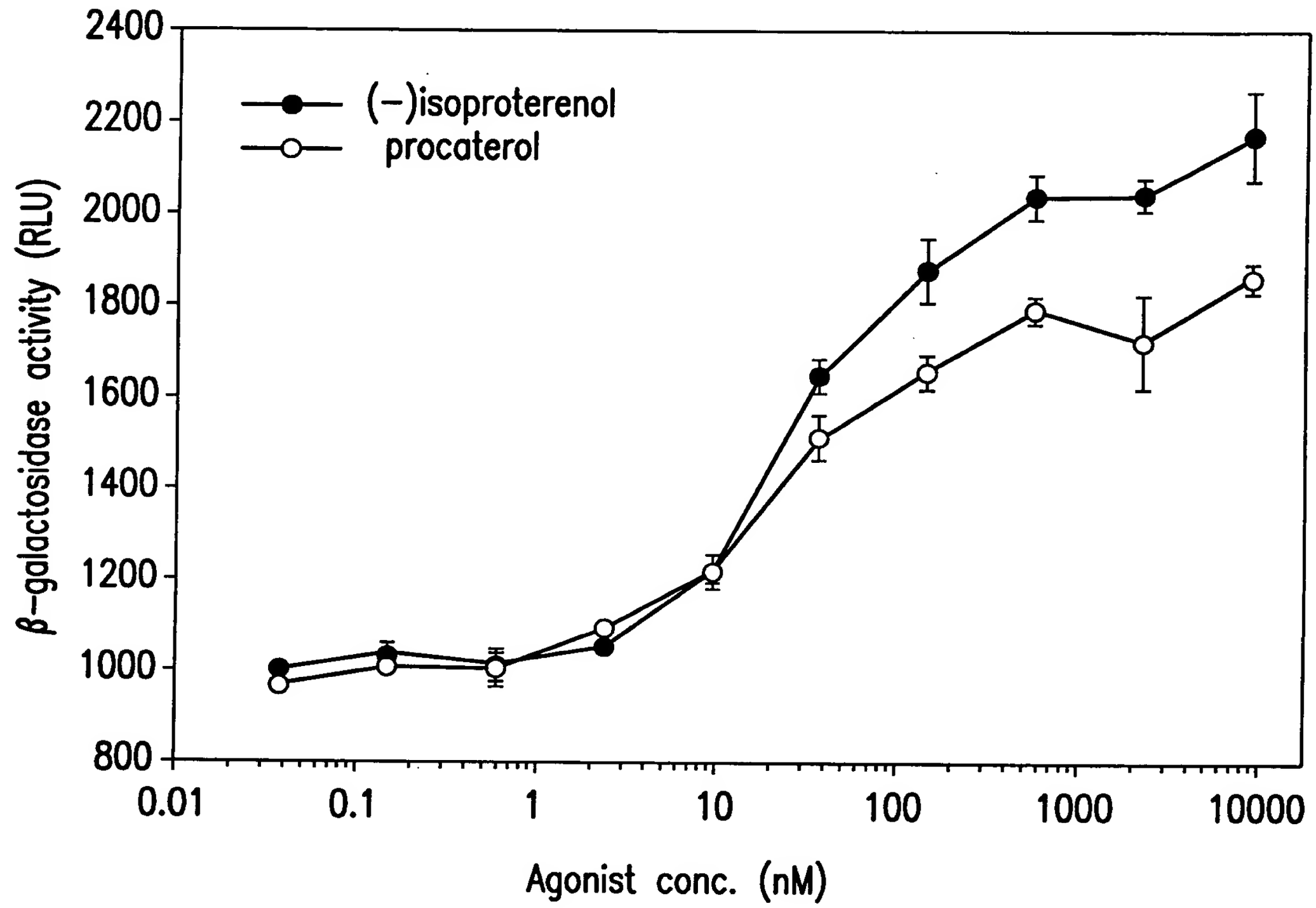


FIG. 4A

β–galactosidase Activity in Response to Agonist in C2 Cells
Coexpressing β2AR–βgalΔα and βArrestin1–βgalΔω Fusion Proteins

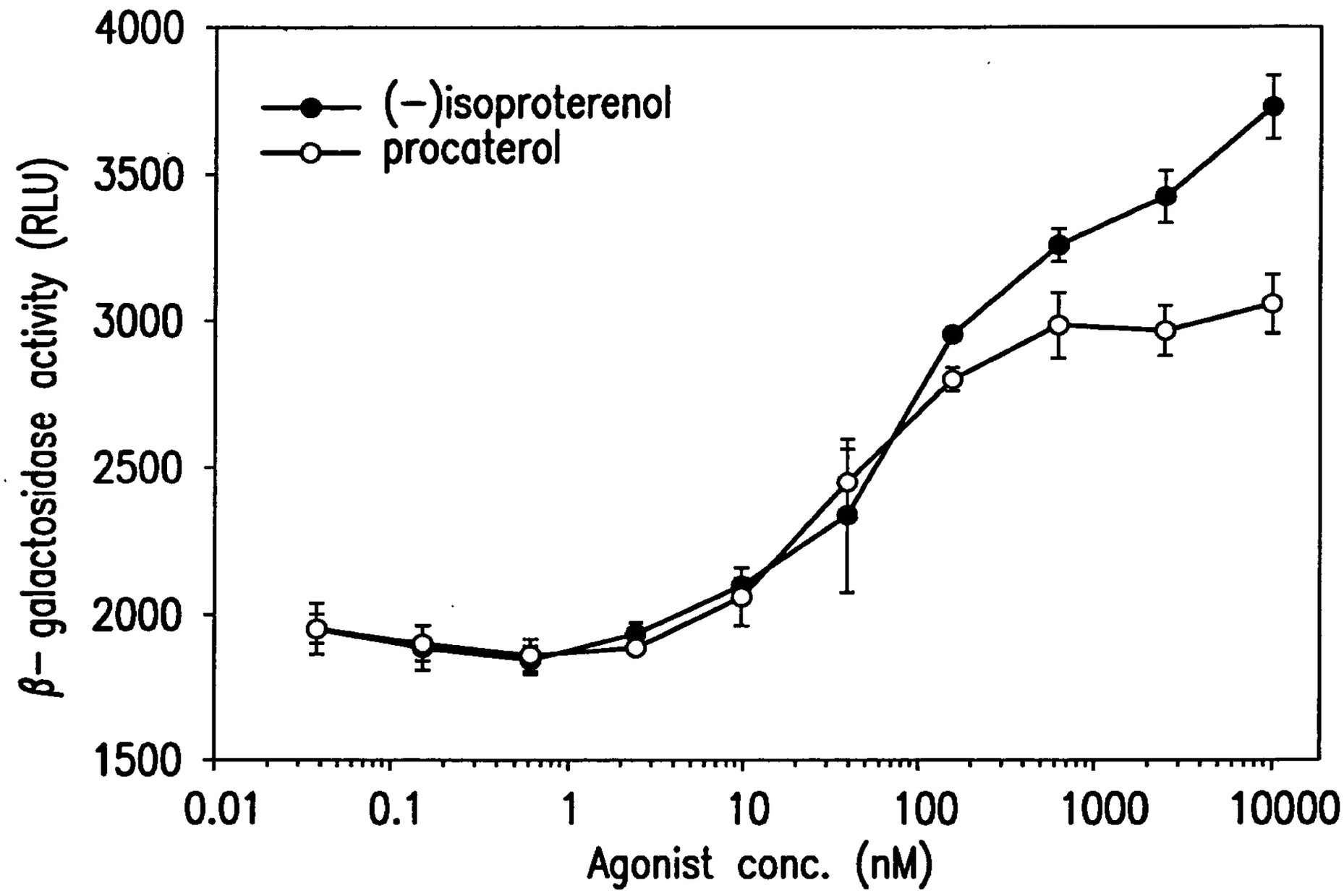


FIG. 4B

Inhibition of β–galactosidase activity in C2 Cells Coexpressing β2AR –βgal Δα and βArrestin2– βgal Δω Fusion Proteins

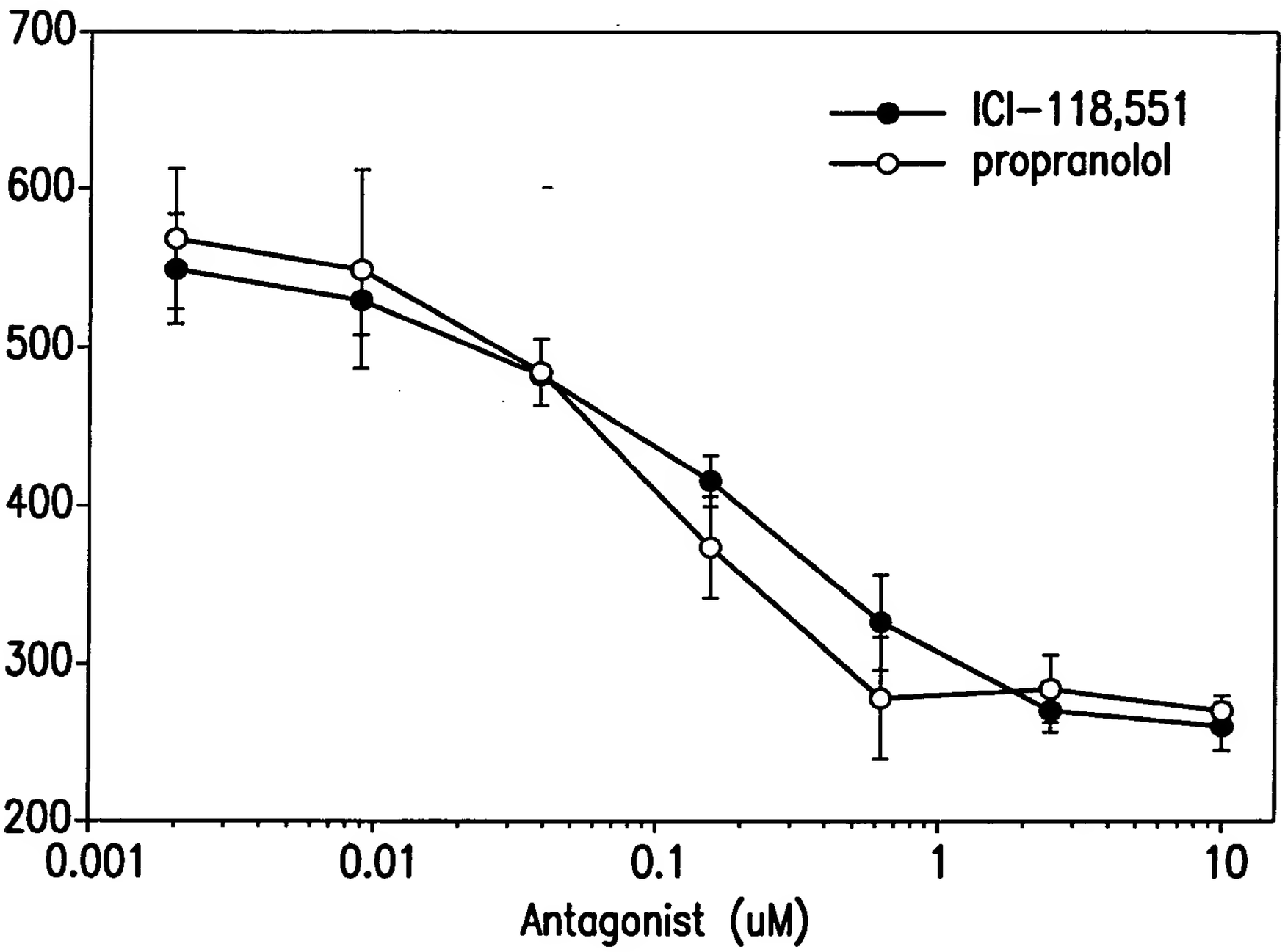


FIG. 5A

Antagonist Inhibition of β-galactosidase Activity in C2 Cells
Coexpressing β2AR-βgalΔα and βArrestin1-βgalΔω Fusion Proteins

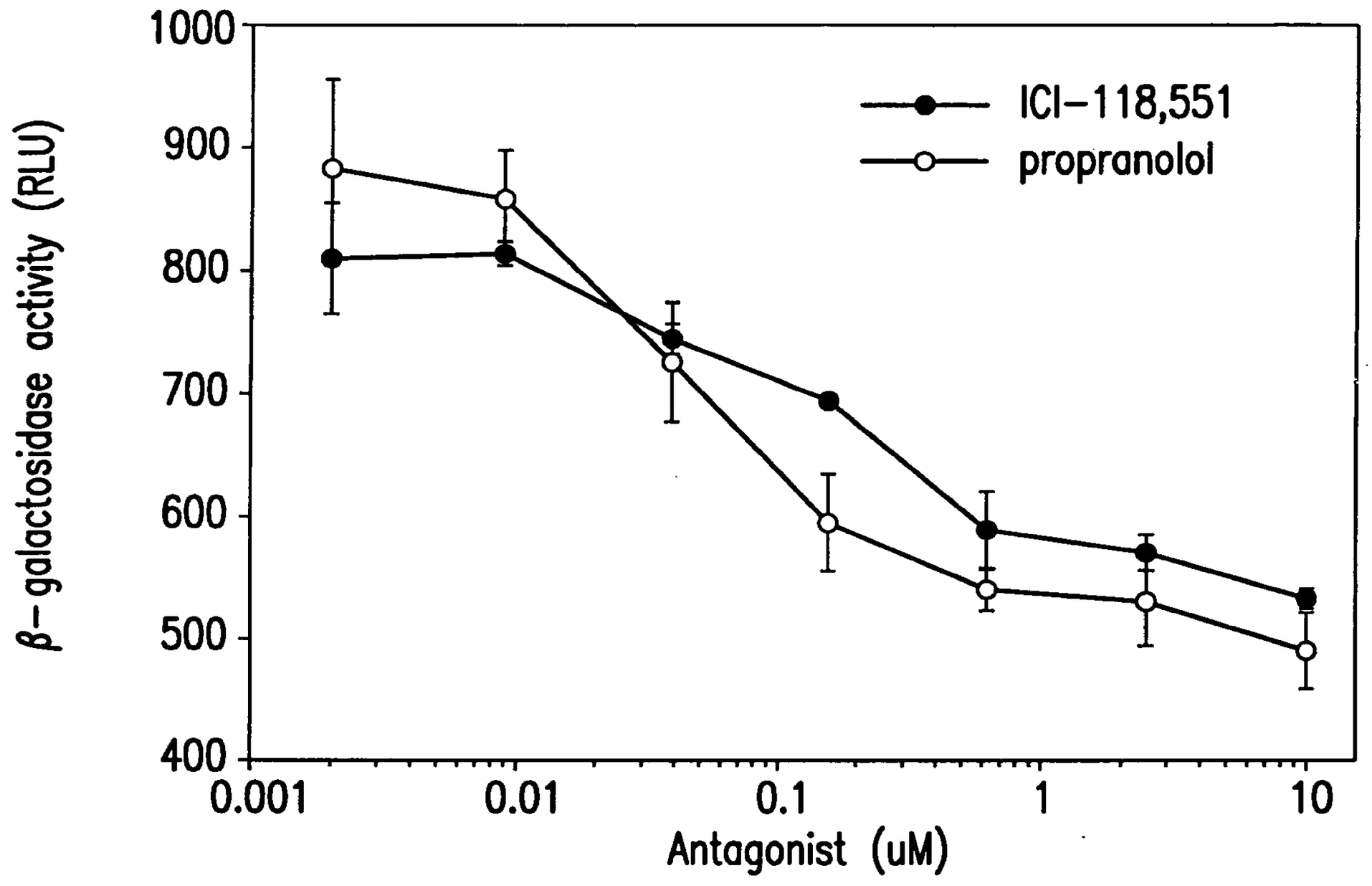


FIG. 5B

Agonist Stimulated cAMP Response in Clones or Pools of C2 Cells Coexpressing A2aR–βgal Δα and βArrestin1– βgal Δω Fusion Proteins

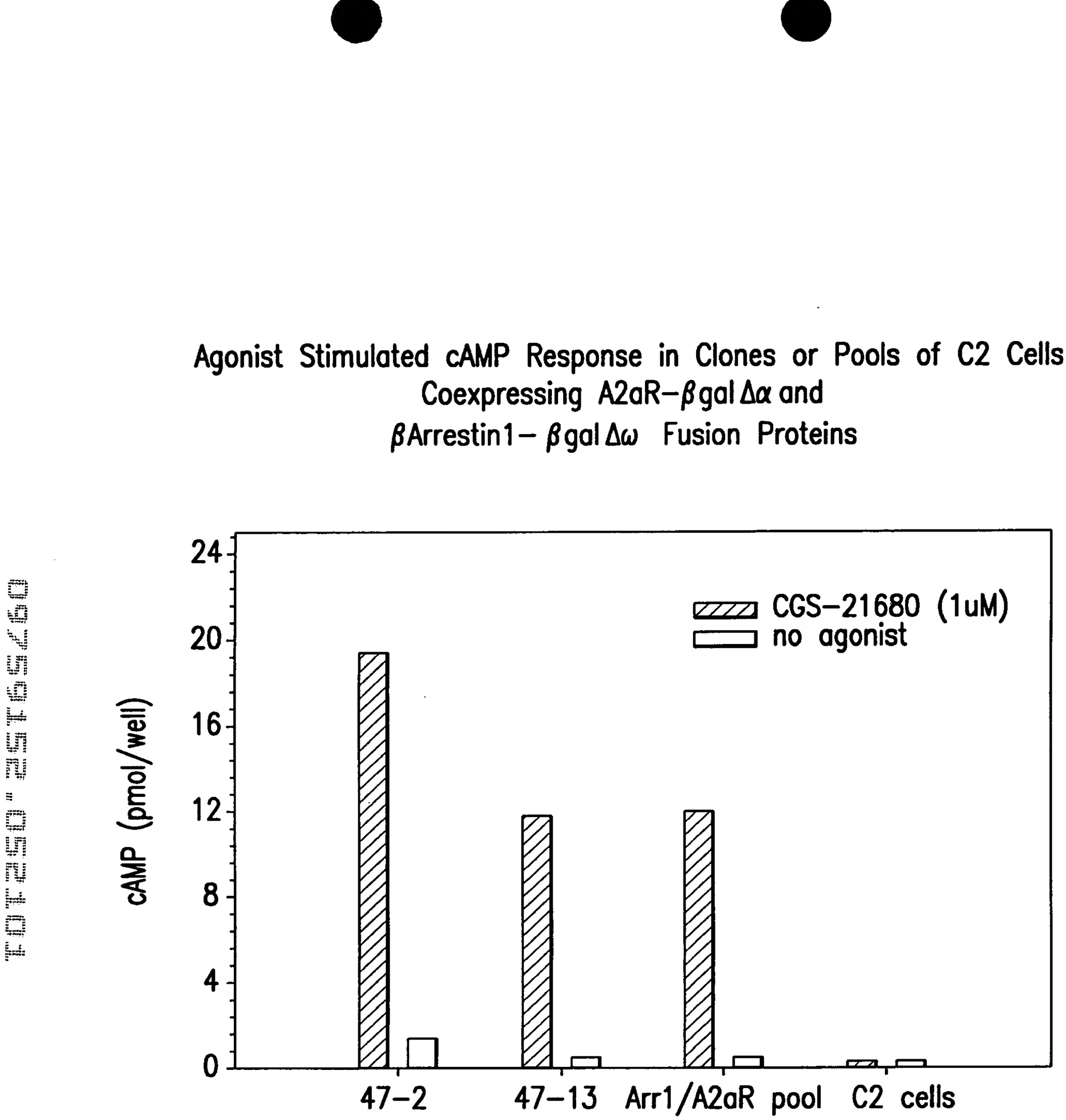


FIG.6

Agonist Stimulated cAMP Response in Clones or Pools of C2 Cells Expressing D1–βgal Δα and βArrestin2–βgal Δω Fusion Proteins

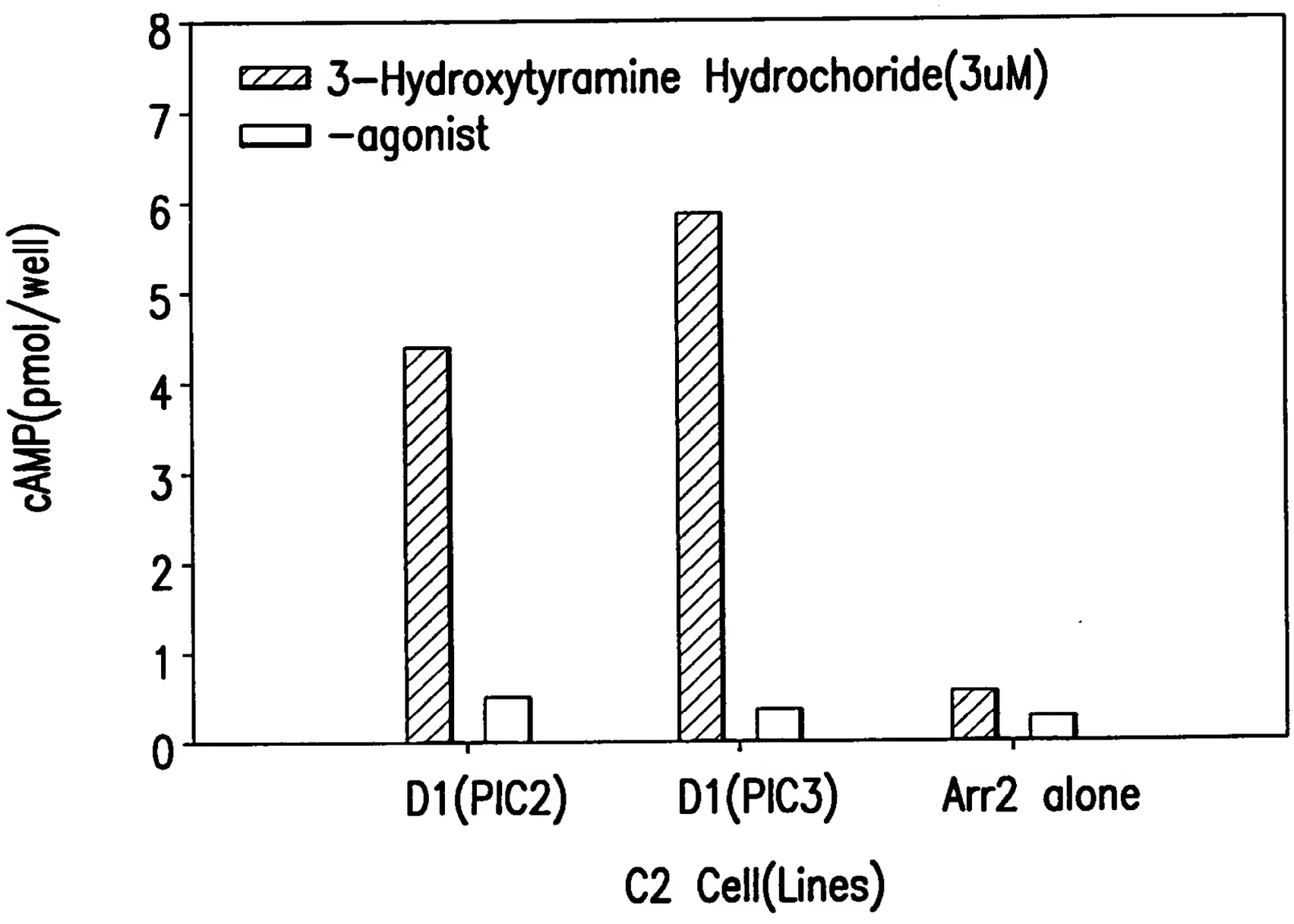


FIG. 7

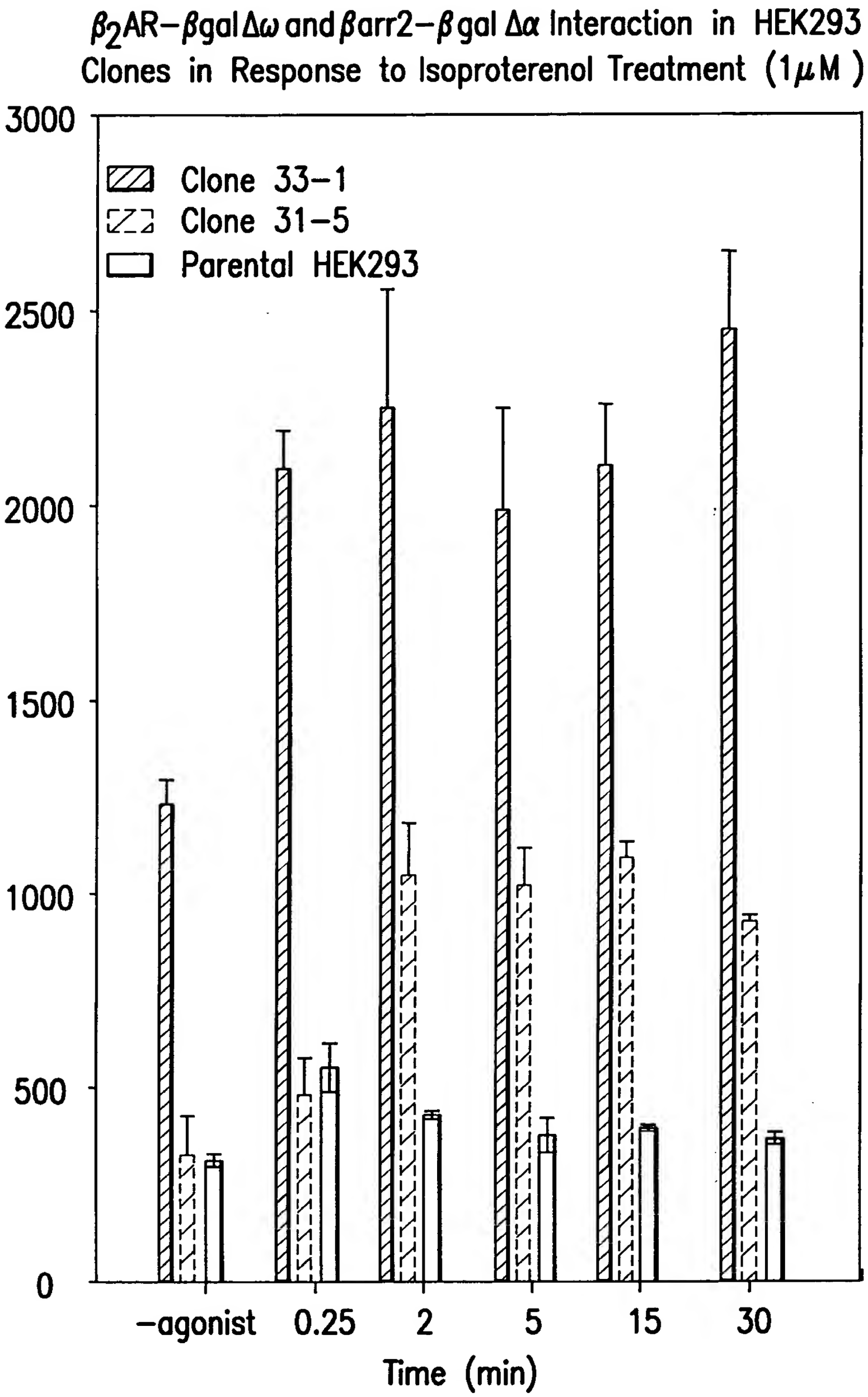

β_2AR–βgal $\Delta\omega$ and βarr2–βgal $\Delta\alpha$ Interaction in HEK293 Clones in Response to Isoproterenol Treatment (1μM)
Clone 33–1
Clone 31–5
Parental HEK293
βgal Activity (RLU)
3000
2500
2000
1500
1000
500
0
–agonist
0.25
2
5
15
30
Time (min)

FIG. 8A

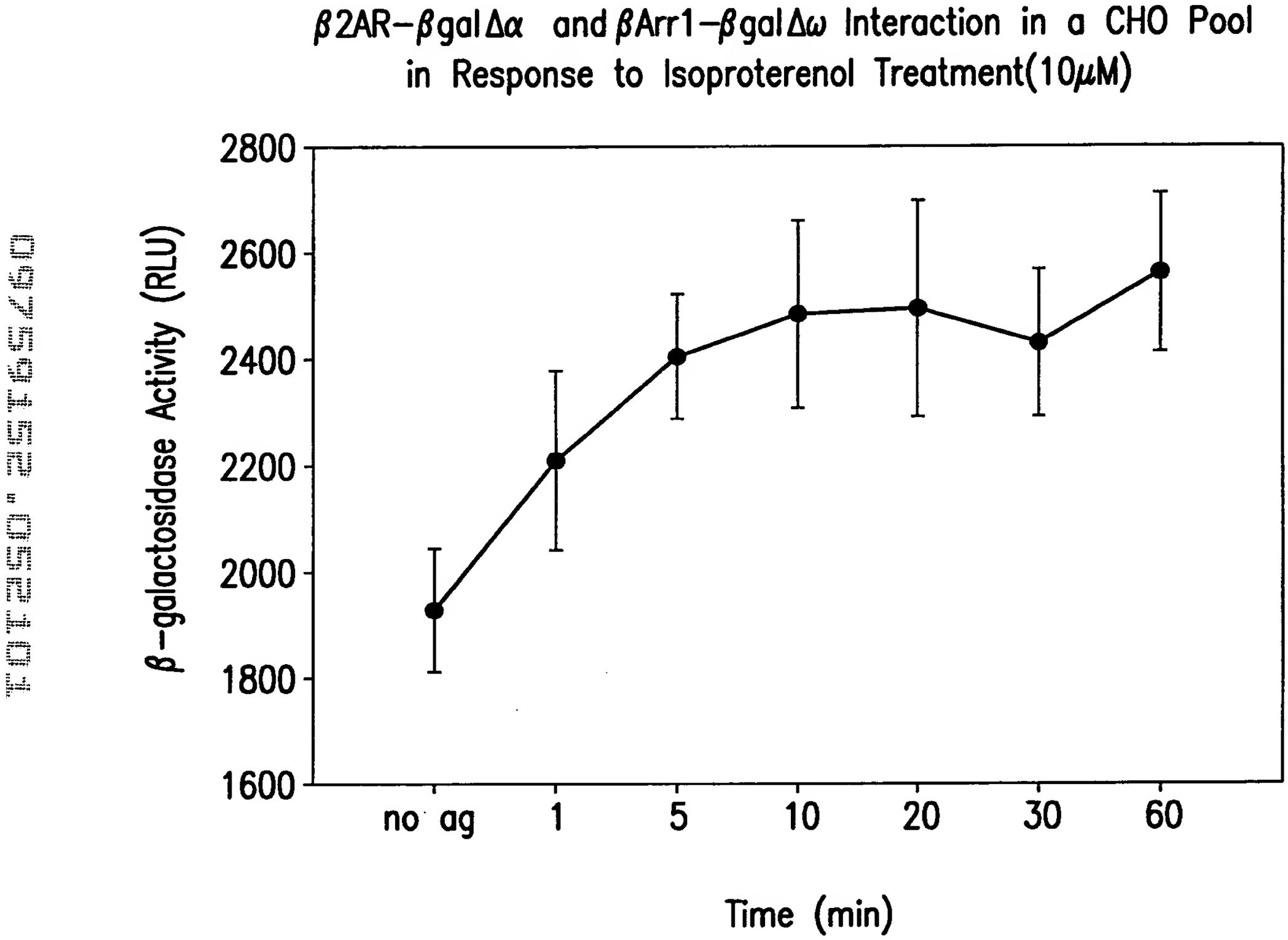

β2AR−βgalΔα and βArr1−βgalΔω Interaction in a CHO Pool
in Response to Isoproterenol Treatment(10μM)
β-galactosidase Activity (RLU)
2800
2600
2400
2200
2000
1800
1600
no ag
1
5
10
20
30
60
Time (min)

FIG. 8B

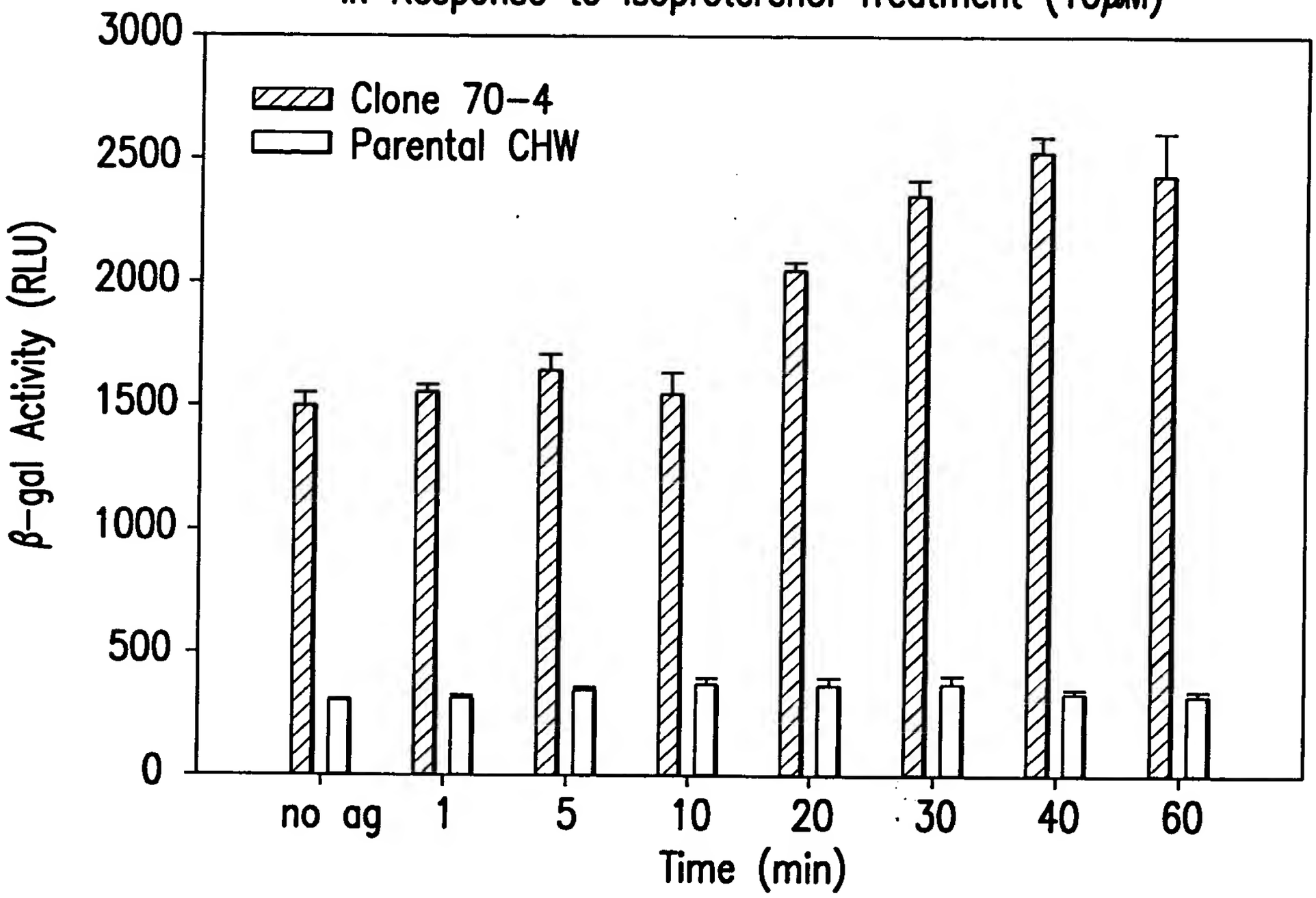

β2AR–βgal Δα and βArr2–βgal Δω Interaction in CHW Clone
in Response to Isoproterenol Treatment (10μM)
Clone 70–4
Parental CHW
β-gal Activity (RLU)
3000
2500
2000
1500
1000
500
0
no ag
1
5
10
20
30
40
60
Time (min)

FIG. 8C

β–galactosidase Complementation as a Measurement for Adrenergic Receptor Homodimerization in HEK 293 Cells Coexpressing β2AR–βgal Δα and β2AR–βgal Δω.

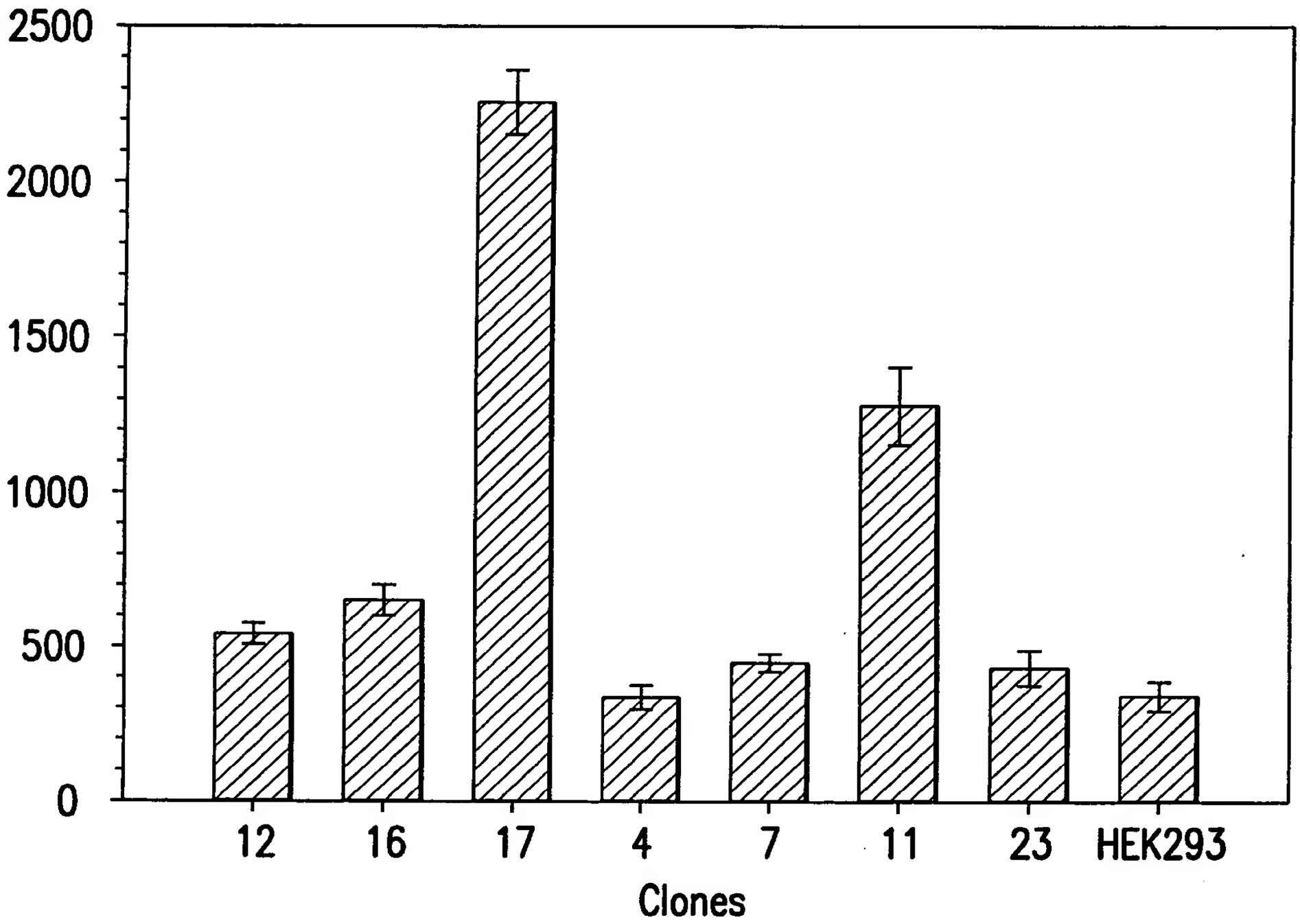


FIG. 9A

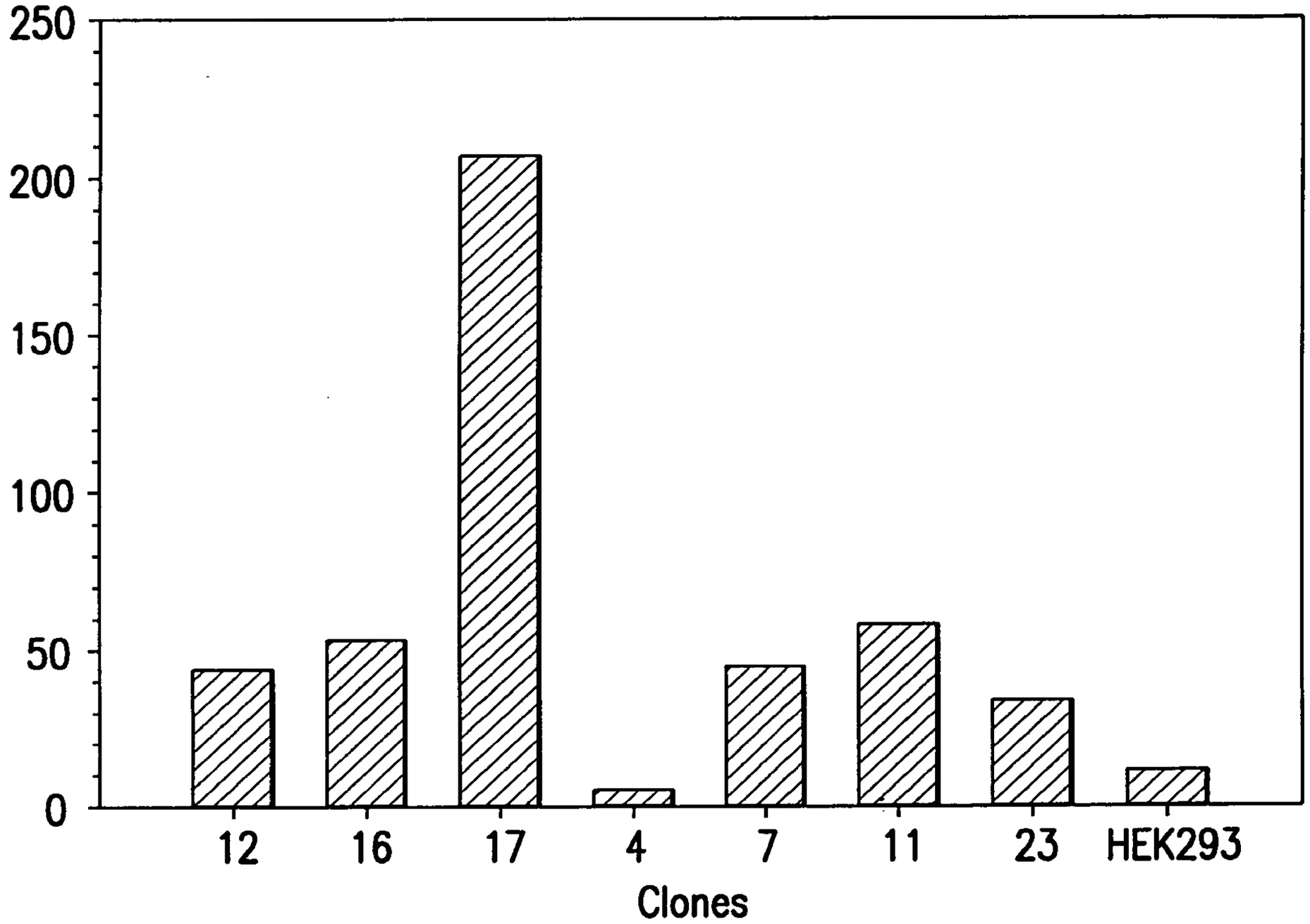

Agonist Stimulated cAMP Response in HEK 293 Cells
Coexpressing β2AR–βgal Δα and β2AR–βgal Δω
cAMP (pmol/well)
250
200
150
100
50
0
12
16
17
4
7
11
23
HEK293
Clones

FIG. 9B

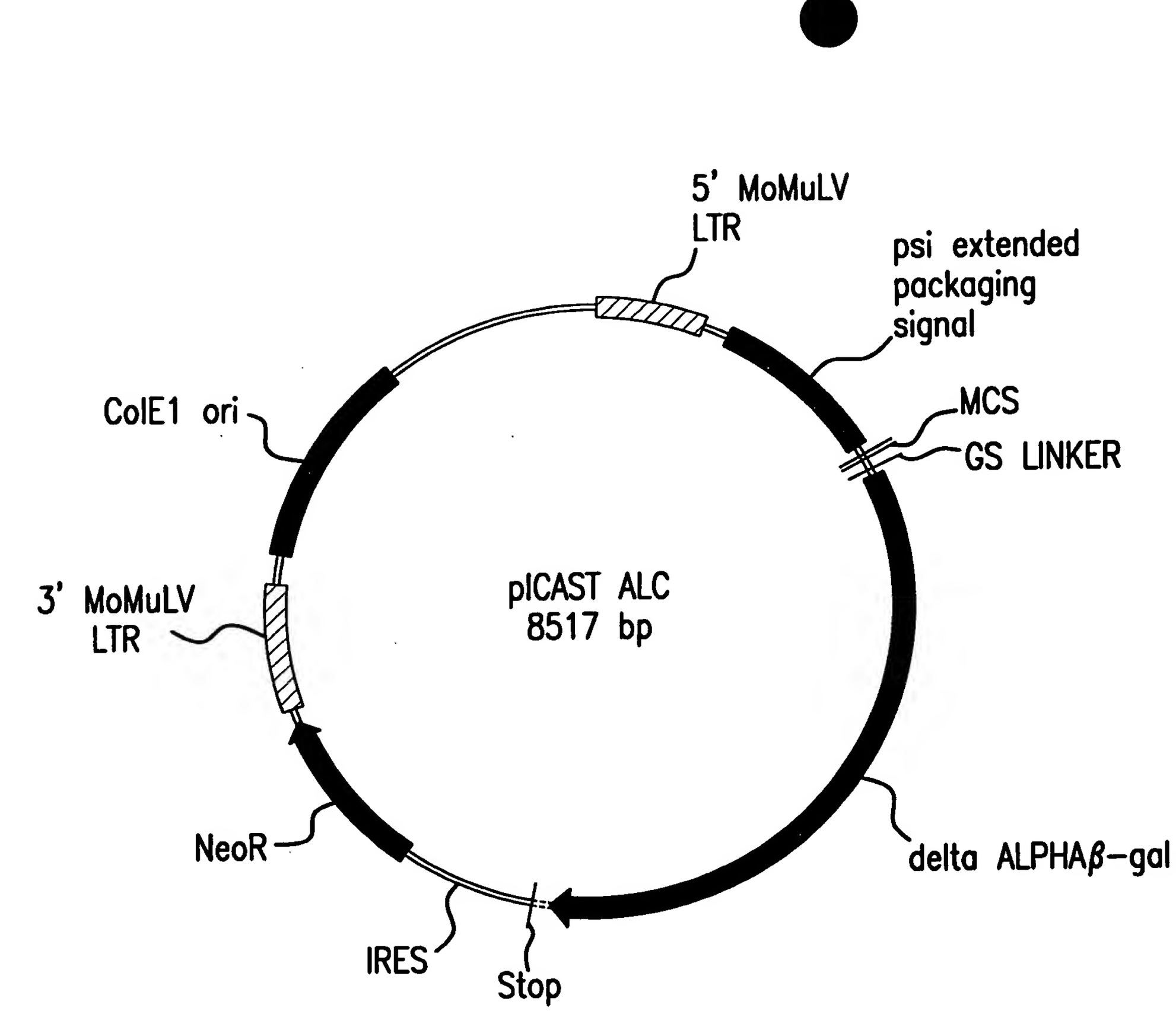


FIG.10A

pICAST ALC

```
   1  CTGCAGCCTG AATATGGGCC AAACAGGATA TCTGTGGTAA GCAGTTCCTG
      GACGTCGGAC TTATACCCGG TTTGTCCTAT AGACACCATT CGTCAAGGAC

  51  CCCCGGCTCA GGGCCAAGAA CAGATGGAAC AGCTGAATAT GGGCCAAACA
      GGGGCCGAGT CCCGGTTCTT GTCTACCTTG TCGACTTATA CCCGGTTTGT

 101  GGATATCTGT GGTAAGCAGT TCCTGCCCCG GCTCAGGGCC AAGAACAGAT
      CCTATAGACA CCATTCGTCA AGGACGGGGC CGAGTCCCGG TTCTTGTCTA

 151  GGTCCCCAGA TGCGGTCCAG CCCTCAGCAG TTTCTAGAGA ACCATCAGAT
      CCAGGGGTCT ACGCCAGGTC GGGAGTCGTC AAAGATCTCT TGGTAGTCTA

 201  GTTTCCAGGG TGCCCCAAGG ACCTGAAATG ACCCTGTGCC TTATTTGAAC
      CAAAGGTCCC ACGGGGTTCC TGGACTTTAC TGGGACACGG AATAAACTTG

 251  TAACCAATCA GTTCGCTTCT CGCTTCTGTT CGCGCGCTTC TGCTCCCCGA
      ATTGGTTAGT CAAGCGAAGA GCGAAGACAA GCGCGCGAAG ACGAGGGGCT

 301  GCTCAATAAA AGAGCCCACA ACCCCTCACT CGGGGCGCCA GTCCTCCGAT
      CGAGTTATTT TCTCGGGTGT TGGGGAGTGA GCCCCGCGGT CAGGAGGCTA

 351  TGACTGAGTC GCCCGGGTAC CCGTGTATCC AATAAACCCT CTTGCAGTTG
      ACTGACTCAG CGGGCCCATG GGCACATAGG TTATTTGGGA GAACGTCAAC

 401  CATCCGACTT GTGGTCTCGC TGTTCCTTGG GAGGGTCTCC TCTGAGTGAT
      GTAGGCTGAA CACCAGAGCG ACAAGGAACC CTCCCAGAGG AGACTCACTA

 451  TGACTACCCG TCAGCGGGGG TCTTTCATTT GGGGGCTCGT CCGGGATCGG
      ACTGATGGGC AGTCGCCCCC AGAAAGTAAA CCCCCGAGCA GGCCCTAGCC

 501  GAGACCCCTG CCCAGGGACC ACCGACCCAC CACCGGGAGG CAAGCTGGCC
      CTCTGGGGAC GGGTCCCTGG TGGCTGGGTG GTGGCCCTCC GTTCGACCGG

 551  AGCAACTTAT CTGTGTCTGT CCGATTGTCT AGTGTCTATG ACTGATTTTA
      TCGTTGAATA GACACAGACA GGCTAACAGA TCACAGATAC TGACTAAAAT

 601  TGCGCCTGCG TCGGTACTAG TTAGCTAACT AGCTCTGTAT CTGGCGGACC
      ACGCGGACGC AGCCATGATC AATCGATTGA TCGAGACATA GACCGCCTGG
```

FIG.10B-1

pICAST ALC

651 CGTGGTGGAA CTGACGAGTT CTGAACACCC GGCCGCAACC CTGGGAGACG
GCACCACCTT GACTGCTCAA GACTTGTGGG CCGGCGTTGG GACCCTCTGC

701 TCCCAGGGAC TTTGGGGGCC GTTTTTGTGG CCCGACCTGA GGAAGGGAGT
AGGGTCCCTG AAACCCCCGG CAAAAACACC GGGCTGGACT CCTTCCCTCA

751 CGATGTGGAA TCCGACCCCG TCAGGATATG TGGTTCTGGT AGGAGACGAG
GCTACACCTT AGGCTGGGGC AGTCCTATAC ACCAAGACCA TCCTCTGCTC

801 AACCTAAAAC AGTTCCCGCC TCCGTCTGAA TTTTTGCTTT CGGTTTGGAA
TTGGATTTTG TCAAGGGCGG AGGCAGACTT AAAAACGAAA GCCAAACCTT

851 CCGAAGCCGC GCGTCTTGTC TGCTGCAGCA TCGTTCTGTG TTGTCTCTGT
GGCTTCGGCG CGCAGAACAG ACGACGTCGT AGCAAGACAC AACAGAGACA

901 CTGACTGTGT TTCTGTATTT GTCTGAAAAT TAGGGCCAGA CTGTTACCAC
GACTGACACA AAGACATAAA CAGACTTTTA ATCCCGGTCT GACAATGGTG

951 TCCCTTAAGT TTGACCTTAG GTAACTGGAA AGATGTCGAG CGGCTCGCTC
AGGGAATTCA AACTGGAATC CATTGACCTT TCTACAGCTC GCCGAGCGAG

1001 ACAACCAGTC GGTAGATGTC AAGAAGAGAC GTTGGGTTAC CTTCTGCTCT
TGTTGGTCAG CCATCTACAG TTCTTCTCTG CAACCCAATG GAAGACGAGA

1051 GCAGAATGGC CAACCTTTAA CGTCGGATGG CCGCGAGACG GCACCTTTAA
CGTCTTACCG GTTGGAAATT GCAGCCTACC GGCGCTCTGC CGTGGAAATT

1101 CCGAGACCTC ATCACCCAGG TTAAGATCAA GGTCTTTTCA CCTGGCCCGC
GGCTCTGGAG TAGTGGGTCC AATTCTAGTT CCAGAAAAGT GGACCGGGCG

1151 ATGGACACCC AGACCAGGTC CCCTACATCG TGACCTGGGA AGCCTTGGCT
TACCTGTGGG TCTGGTCCAG GGGATGTAGC ACTGGACCCT TCGGAACCGA

1201 TTTGACCCCC CTCCCTGGGT CAAGCCCTTT GTACACCCTA AGCCTCCGCC
AAACTGGGGG GAGGGACCCA GTTCGGGAAA CATGTGGGAT TCGGAGGCGG

1251 TCCTCTTCCT CCATCCGCCC CGTCTCTCCC CCTTGAACCT CCTCGTTCGA
AGGAGAAGGA GGTAGGCGGG GCAGAGAGGG GGAACTTGGA GGAGCAAGCT

FIG.10B-2

pICAST ALC

```
1301    CCCCGCCTCG ATCCTCCCTT TATCCAGCCC TCACTCCTTC TCTAGGCGCC
        GGGGCGGAGC TAGGAGGGAA ATAGGTCGGG AGTGAGGAAG AGATCCGCGG

1351    GGCCGCTCTA GCCCATTAAT ACGACTCACT ATAGGGCGAT TCGAATCAGG
        CCGGCGAGAT CGGGTAATTA TGCTGAGTGA TATCCCGCTA AGCTTAGTCC

1401    CCTTGGCGCG CCGGATCCTT AATTAAGCGC AATTGGGAGG TGGCGGTAGC
        GGAACCGCGC GGCCTAGGAA TTAATTCGCG TTAACCCTCC ACCGCCATCG

+2              M  G   V  I  T   D  S  L   A  V  V  A   R  T  D
               ]----------------------------------------------

1451    CTCGAGATGG GCGTGATTAC GGATTCACTG GCCGTCGTGG CCCGCACCGA
        GAGCTCTACC CGCACTAATG CCTAAGTGAC CGGCAGCACC GGGCGTGGCT

+2        R  P  S   Q  Q  L  R   S  L  N   G  E  W   R  F  A
          ----------------------------------------------------

1501    TCGCCCTTCC CAACAGTTAC GCAGCCTGAA TGGCGAATGG CGCTTTGCCT
        AGCGGGAAGG GTTGTCAATG CGTCGGACTT ACCGCTTACC GCGAAACGGA

+2      W  F  P  A   P  E  A   V  P  E  S   W  L  E   C  D  L
        ----------------------------------------------------

1551    GGTTTCCGGC ACCAGAAGCG GTGCCGGAAA GCTGGCTGGA GTGCGATCTT
        CCAAAGGCCG TGGTCTTCGC CACGGCCTTT CGACCGACCT CACGCTAGAA

+2        P  E  A  D   T  V  V   V  P  S   N  W  Q  M   H  G  Y
          ----------------------------------------------------

1601    CCTGAGGCCG ATACTGTCGT CGTCCCCTCA AACTGGCAGA TGCACGGTTA
        GGACTCCGGC TATGACAGCA GCAGGGGAGT TTGACCGTCT ACGTGCCAAT

+2          D  A  P   I  Y  T  N   V  T  Y   P  I  T   V  N  P
            ----------------------------------------------------

1651    CGATGCGCCC ATCTACACCA ACGTGACCTA TCCCATTACG GTCAATCCGC
        GCTACGCGGG TAGATGTGGT TGCACTGGAT AGGGTAATGC CAGTTAGGCG

+2      P  F  V  P   T  E  N   P  T  G  C   Y  S  L   T  F  N
        ----------------------------------------------------

1701    CGTTTGTTCC CACGGAGAAT CCGACGGGTT GTTACTCGCT CACATTTAAT
        GCAAACAAGG GTGCCTCTTA GGCTGCCCAA CAATGAGCGA GTGTAAATTA
```

FIG.10B-3

pICAST ALC

```
+2      V  D  E  S   W  L  Q   E  G  Q   T  R  I  I   F  D  G
        ---------------------------------------------------
1751    GTTGATGAAA GCTGGCTACA GGAAGGCCAG ACGCGAATTA TTTTTGATGG
        CAACTACTTT CGACCGATGT CCTTCCGGTC TGCGCTTAAT AAAAACTACC

+2      V  N  S   A  F  H  L   W  C  N   G  R  W   V  G  Y
        ---------------------------------------------------
1801    CGTTAACTCG GCGTTTCATC TGTGGTGCAA CGGGCGCTGG GTCGGTTACG
        GCAATTGAGC CGCAAAGTAG ACACCACGTT GCCCGCGACC CAGCCAATGC

+2      G  Q  D  S   R  L  P   S  E  F  D   L  S  A   F  L  R
        ---------------------------------------------------
1851    GCCAGGACAG TCGTTTGCCG TCTGAATTTG ACCTGAGCGC ATTTTTACGC
        CGGTCCTGTC AGCAAACGGC AGACTTAAAC TGGACTCGCG TAAAAATGCG

+2      A  G  E  N   R  L  A   V  M  V   L  R  W  S   D  G  S
        ---------------------------------------------------
1901    GCCGGAGAAA ACCGCCTCGC GGTGATGGTG CTGCGCTGGA GTGACGGCAG
        CGGCCTCTTT TGGCGGAGCG CCACTACCAC GACGCGACCT CACTGCCGTC

+2      Y  L  E   D  Q  D  M   W  R  M   S  G  I   F  R  D
        ---------------------------------------------------
1951    TTATCTGGAA GATCAGGATA TGTGGCGGAT GAGCGGCATT TTCCGTGACG
        AATAGACCTT CTAGTCCTAT ACACCGCCTA CTCGCCGTAA AAGGCACTGC

+2      V  S  L  L   H  K  P   T  T  Q  I   S  D  F   H  V  A
        ---------------------------------------------------
2001    TCTCGTTGCT GCATAAACCG ACTACACAAA TCAGCGATTT CCATGTTGCC
        AGAGCAACGA CGTATTTGGC TGATGTGTTT AGTCGCTAAA GGTACAACGG

+2      T  R  F  N   D  D  F   S  R  A   V  L  E  A   E  V  Q
        ---------------------------------------------------
2051    ACTCGCTTTA ATGATGATTT CAGCCGCGCT GTACTGGAGG CTGAAGTTCA
        TGAGCGAAAT TACTACTAAA GTCGGCGCGA CATGACCTCC GACTTCAAGT
```

FIG.10B-4

pICAST ALC

```
+2          M  C  G   E  L  R  D   Y  L  R   V  T  V   S  L  W
           ----------------------------------------------------
2101   GATGTGCGGC GAGTTGCGTG ACTACCTACG GGTAACAGTT TCTTTATGGC
       CTACACGCCG CTCAACGCAC TGATGGATGC CCATTGTCAA AGAAATACCG

+2     Q  G  E  T   Q  V  A   S  G  T  A   P  F  G   G  E  I
       ----------------------------------------------------
2151   AGGGTGAAAC GCAGGTCGCC AGCGGCACCG CGCCTTTCGG CGGTGAAATT
       TCCCACTTTG CGTCCAGCGG TCGCCGTGGC GCGGAAAGCC GCCACTTTAA

+2          I  D  E  R   G  G  Y   A  D  R   V  T  L  R   L  N  V
           -------------------------------------------------------
2201   ATCGATGAGC GTGGTGGTTA TGCCGATCGC GTCACACTAC GTCTGAACGT
       TAGCTACTCG CACCACCAAT ACGGCTAGCG CAGTGTGATG CAGACTTGCA

+2          E  N  P   K  L  W  S   A  E  I   P  N  L   Y  R  A
           -------------------------------------------------------
2251   CGAAAACCCG AAACTGTGGA GCGCCGAAAT CCCGAATCTC TATCGTGCGG
       GCTTTTGGGC TTTGACACCT CGCGGCTTTA GGGCTTAGAG ATAGCACGCC

+2     V  V  E  L   H  T  A   D  G  T  L   I  E  A   E  A  C
       ----------------------------------------------------
2301   TGGTTGAACT GCACACCGCC GACGGCACGC TGATTGAAGC AGAAGCCTGC
       ACCAACTTGA CGTGTGGCGG CTGCCGTGCG ACTAACTTCG TCTTCGGACG

+2          D  V  G  F   R  E  V   R  I  E   N  G  L  L   L  L  N
           -------------------------------------------------------
2351   GATGTCGGTT TCCGCGAGGT GCGGATTGAA AATGGTCTGC TGCTGCTGAA
       CTACAGCCAA AGGCGCTCCA CGCCTAACTT TTACCAGACG ACGACGACTT

+2          G  K  P   L  L  I  R   G  V  N   R  H  E   H  H  P
           -------------------------------------------------------
2401   CGGCAAGCCG TTGCTGATTC GAGGCGTTAA CCGTCACGAG CATCATCCTC
       GCCGTTCGGC AACGACTAAG CTCCGCAATT GGCAGTGCTC GTAGTAGGAG
```

FIG.10B-5

pICAST ALC

```
+2      L  H  G  Q   V  M  D   E  Q  T  M   V  Q  D   I  L  L
        ------------------------------------------------------
2451    TGCATGGTCA GGTCATGGAT GAGCAGACGA TGGTGCAGGA TATCCTGCTG
        ACGTACCAGT CCAGTACCTA CTCGTCTGCT ACCACGTCCT ATAGGACGAC

+2       M  K  Q  N   N  F  N   A  V  R   C  S  H  Y   P  N  H
        ------------------------------------------------------
2501    ATGAAGCAGA ACAACTTTAA CGCCGTGCGC TGTTCGCATT ATCCGAACCA
        TACTTCGTCT TGTTGAAATT GCGGCACGCG ACAAGCGTAA TAGGCTTGGT

+2        P  L  W   Y  T  L  C   D  R  Y   G  L  Y   V  V  D
        ------------------------------------------------------
2551    TCCGCTGTGG TACACGCTGT GCGACCGCTA CGGCCTGTAT GTGGTGGATG
        AGGCGACACC ATGTGCGACA CGCTGGCGAT GCCGGACATA CACCACCTAC

+2      E  A  N  I   E  T  H   G  M  V  P   M  N  R   L  T  D
        ------------------------------------------------------
2601    AAGCCAATAT TGAAACCCAC GGCATGGTGC CAATGAATCG TCTGACCGAT
        TTCGGTTATA ACTTTGGGTG CCGTACCACG GTTACTTAGC AGACTGGCTA

+2       D  P  R  W   L  P  A   M  S  E   R  V  T  R   M  V  Q
        ------------------------------------------------------
2651    GATCCGCGCT GGCTACCGGC GATGAGCGAA CGCGTAACGC GAATGGTGCA
        CTAGGCGCGA CCGATGGCCG CTACTCGCTT GCGCATTGCG CTTACCACGT

+2        R  D  R   N  H  P  S   V  I  I   W  S  L   G  N  E
        ------------------------------------------------------
2701    GCGCGATCGT AATCACCCGA GTGTGATCAT CTGGTCGCTG GGGAATGAAT
        CGCGCTAGCA TTAGTGGGCT CACACTAGTA GACCAGCGAC CCCTTACTTA

+2      S  G  H  G   A  N  H   D  A  L  Y   R  W  I   K  S  V
        ------------------------------------------------------
2751    CAGGCCACGG CGCTAATCAC GACGCGCTGT ATCGCTGGAT CAAATCTGTC
        GTCCGGTGCC GCGATTAGTG CTGCGCGACA TAGCGACCTA GTTTAGACAG
```

FIG.10B-6

pICAST ALC

```
+2      D  P  S  R   P  V  Q   Y  E  G   G  G  A  D   T  T  A
        ----------------------------------------------------
2801    GATCCTTCCC GCCCGGTGCA GTATGAAGGC GGCGGAGCCG ACACCACGGC
        CTAGGAAGGG CGGGCCACGT CATACTTCCG CCGCCTCGGC TGTGGTGCCG

+2        T  D  I   I  C  P  M   Y  A  R   V  D  E   D  Q  P
          ----------------------------------------------------
2851    CACCGATATT ATTTGCCCGA TGTACGCGCG CGTGGATGAA GACCAGCCCT
        GTGGCTATAA TAAACGGGCT ACATGCGCGC GCACCTACTT CTGGTCGGGA

+2      F  P  A  V   P  K  W   S  I  K  K   W  L  S   L  P  G
        ----------------------------------------------------
2901    TCCCGGCTGT GCCGAAATGG TCCATCAAAA AATGGCTTTC GCTACCTGGA
        AGGGCCGACA CGGCTTTACC AGGTAGTTTT TTACCGAAAG CGATGGACCT

+2        E  T  R  P   L  I  L   C  E  Y   A  H  A  M   G  N  S
          ----------------------------------------------------
2951    GAGACGCGCC CGCTGATCCT TTGCGAATAC GCCCACGCGA TGGGTAACAG
        CTCTGCGCGG GCGACTAGGA AACGCTTATG CGGGTGCGCT ACCCATTGTC

+2        L  G  G   F  A  K  Y   W  Q  A   F  R  Q   Y  P  R
          ----------------------------------------------------
3001    TCTTGGCGGT TTCGCTAAAT ACTGGCAGGC GTTTCGTCAG TATCCCCGTT
        AGAACCGCCA AAGCGATTTA TGACCGTCCG CAAAGCAGTC ATAGGGGCAA

+2      L  Q  G  G   F  V  W   D  W  V  D   Q  S  L   I  K  Y
        ----------------------------------------------------
3051    TACAGGGCGG CTTCGTCTGG GACTGGGTGG ATCAGTCGCT GATTAAATAT
        ATGTCCCGCC GAAGCAGACC CTGACCCACC TAGTCAGCGA CTAATTTATA

+2        D  E  N  G   N  P  W   S  A  Y   G  G  D  F   G  D  T
          ----------------------------------------------------
3101    GATGAAAACG GCAACCCGTG GTCGGCTTAC GGCGGTGATT TTGGCGATAC
        CTACTTTTGC CGTTGGGCAC CAGCCGAATG CCGCCACTAA AACCGCTATG
```

FIG.10B-7

pICAST ALC

```
+2          P  N  D   R  Q  F  C   M  N  G   L  V  F   A  D  R
           ----------------------------------------------------
3151   GCCGAACGAT CGCCAGTTCT GTATGAACGG TCTGGTCTTT GCCGACCGCA
       CGGCTTGCTA GCGGTCAAGA CATACTTGCC AGACCAGAAA CGGCTGGCGT

+2          T  P  H  P   A  L  T   E  A  K  H   Q  Q  Q   F  F  Q
           ----------------------------------------------------
3201   CGCCGCATCC AGCGCTGACG GAAGCAAAAC ACCAGCAGCA GTTTTTCCAG
       GCGGCGTAGG TCGCGACTGC CTTCGTTTTG TGGTCGTCGT CAAAAAGGTC

+2          F  R  L  S   G  Q  T   I  E  V   T  S  E  Y   L  F  R
           ----------------------------------------------------
3251   TTCCGTTTAT CCGGGCAAAC CATCGAAGTG ACCAGCGAAT ACCTGTTCCG
       AAGGCAAATA GGCCCGTTTG GTAGCTTCAC TGGTCGCTTA TGGACAAGGC

+2          H  S  D   N  E  L  L   H  W  M   V  A  L   D  G  K
           ----------------------------------------------------
3301   TCATAGCGAT AACGAGCTCC TGCACTGGAT GGTGGCGCTG GATGGTAAGC
       AGTATCGCTA TTGCTCGAGG ACGTGACCTA CCACCGCGAC CTACCATTCG

+2          P  L  A  S   G  E  V   P  L  D  V   A  P  Q   G  K  Q
           ----------------------------------------------------
3351   CGCTGGCAAG CGGTGAAGTG CCTCTGGATG TCGCTCCACA AGGTAAACAG
       GCGACCGTTC GCCACTTCAC GGAGACCTAC AGCGAGGTGT TCCATTTGTC

+2          L  I  E  L   P  E  L   P  Q  P   E  S  A  G   Q  L  W
           ----------------------------------------------------
3401   TTGATTGAAC TGCCTGAACT ACCGCAGCCG GAGAGCGCCG GGCAACTCTG
       AACTAACTTG ACGGACTTGA TGGCGTCGGC CTCTCGCGGC CCGTTGAGAC

+2          L  T  V   R  V  V  Q   P  N  A   T  A  W   S  E  A
           ----------------------------------------------------
3451   GCTCACAGTA CGCGTAGTGC AACCGAACGC GACCGCATGG TCAGAAGCCG
       CGAGTGTCAT GCGCATCACG TTGGCTTGCG CTGGCGTACC AGTCTTCGGC
```

FIG.10B-8

pICAST ALC

```
+2      G  H  I  S   A  W  Q   Q  W  R  L   A  E  N   L  S  V
        ----------------------------------------------------
3501    GGCACATCAG CGCCTGGCAG CAGTGGCGTC TGGCGGAAAA CCTCAGTGTG
        CCGTGTAGTC GCGGACCGTC GTCACCGCAG ACCGCCTTTT GGAGTCACAC

+2       T  L  P  A   A  S  H   A  I  P   H  L  T  T   S  E  M
        ----------------------------------------------------
3551    ACGCTCCCCG CCGCGTCCCA CGCCATCCCG CATCTGACCA CCAGCGAAAT
        TGCGAGGGGC GGCGCAGGGT GCGGTAGGGC GTAGACTGGT GGTCGCTTTA

+2        D  F  C   I  E  L  G   N  K  R   W  Q  F   N  R  Q
        ----------------------------------------------------
3601    GGATTTTTGC ATCGAGCTGG GTAATAAGCG TTGGCAATTT AACCGCCAGT
        CCTAAAAACG TAGCTCGACC CATTATTCGC AACCGTTAAA TTGGCGGTCA

+2      S  G  F  L   S  Q  M   W  I  G  D   K  K  Q   L  L  T
        ----------------------------------------------------
3651    CAGGCTTTCT TTCACAGATG TGGATTGGCG ATAAAAAACA ACTGCTGACG
        GTCCGAAAGA AAGTGTCTAC ACCTAACCGC TATTTTTTGT TGACGACTGC

+2       P  L  R  D   Q  F  T   R  A  P   L  D  N  D   I  G  V
        ----------------------------------------------------
3701    CCGCTGCGCG ATCAGTTCAC CCGTGCACCG CTGGATAACG ACATTGGCGT
        GGCGACGCGC TAGTCAAGTG GGCACGTGGC GACCTATTGC TGTAACCGCA

+2        S  E  A   T  R  I  D   P  N  A   W  V  E   R  W  K
        ----------------------------------------------------
3751    AAGTGAAGCG ACCCGCATTG ACCCTAACGC CTGGGTCGAA CGCTGGAAGG
        TTCACTTCGC TGGGCGTAAC TGGGATTGCG GACCCAGCTT GCGACCTTCC

+2      A  A  G  H   Y  Q  A   E  A  A  L   L  Q  C   T  A  D
        ----------------------------------------------------
3801    CGGCGGGCCA TTACCAGGCC GAAGCAGCGT TGTTGCAGTG CACGGCAGAT
        GCCGCCCGGT AATGGTCCGG CTTCGTCGCA ACAACGTCAC GTGCCGTCTA
```

FIG.10B-9

pICAST ALC

```
+2        T  L  A  D   A  V  L   I  T  T   A  H  A  W   Q  H  Q
          ---------------------------------------------------
3851      ACACTTGCTG ATGCGGTGCT GATTACGACC GCTCACGCGT GGCAGCATCA
          TGTGAACGAC TACGCCACGA CTAATGCTGG CGAGTGCGCA CCGTCGTAGT

+2          G  K  T   L  F  I  S   R  K  T   Y  R  I   D  G  S
          ---------------------------------------------------
3901      GGGGAAAACC TTATTTATCA GCCGGAAAAC CTACCGGATT GATGGTAGTG
          CCCCTTTTGG AATAAATAGT CGGCCTTTTG GATGGCCTAA CTACCATCAC

+2        G  Q  M  A   I  T  V   D  V  E  V   A  S  D   T  P  H
          ---------------------------------------------------
3951      GTCAAATGGC GATTACCGTT GATGTTGAAG TGGCGAGCGA TACACCGCAT
          CAGTTTACCG CTAATGGCAA CTACAACTTC ACCGCTCGCT ATGTGGCGTA

+2        P  A  R  I   G  L  N   C  Q  L   A  Q  V  A   E  R  V
          ---------------------------------------------------
4001      CCGGCGCGGA TTGGCCTGAA CTGCCAGCTG GCGCAGGTAG CAGAGCGGGT
          GGCCGCGCCT AACCGGACTT GACGGTCGAC CGCGTCCATC GTCTCGCCCA

+2          N  W  L   G  L  G  P   Q  E  N   Y  P  D   R  L  T
          ---------------------------------------------------
4051      AAACTGGCTC GGATTAGGGC CGCAAGAAAA CTATCCCGAC CGCCTTACTG
          TTTGACCGAG CCTAATCCCG GCGTTCTTTT GATAGGGCTG GCGGAATGAC

+2        A  A  C  F   D  R  W   D  L  P  L   S  D  M   Y  T  P
          ---------------------------------------------------
4101      CCGCCTGTTT TGACCGCTGG GATCTGCCAT TGTCAGACAT GTATACCCCG
          GGCGGACAAA ACTGGCGACC CTAGACGGTA ACAGTCTGTA CATATGGGGC

+2        T  V  F  P   S  E  N   G  L  R   C  G  T  R   E  L  N
          ---------------------------------------------------
4151      TACGTCTTCC CGAGCGAAAA CGGTCTGCGC TGCGGGACGC GCGAATTGAA
          ATGCAGAAGG GCTCGCTTTT GCCAGACGCG ACGCCCTGCG CGCTTAACTT
```

FIG.10B-10

pICAST ALC

```
+2          Y  G  P   H  Q  W  R   G  D  F   Q  F  N   I  S  R
            ----------------------------------------------------
4201        TTATGGCCCA CACCAGTGGC GCGGCGACTT CCAGTTCAAC ATCAGCCGCT
            AATACCGGGT GTGGTCACCG CGCCGCTGAA GGTCAAGTTG TAGTCGGCGA

+2          Y  S  Q  Q   Q  L  M   E  T  S  H   R  H  L   L  H  A
            ----------------------------------------------------
4251        ACAGTCAACA GCAACTGATG GAAACCAGCC ATCGCCATCT GCTGCACGCG
            TGTCAGTTGT CGTTGACTAC CTTTGGTCGG TAGCGGTAGA CGACGTGCGC

+2           E  E  G  T   W  L  N   I  D  G   F  H  M  G   I  G  G
            ----------------------------------------------------
4301        GAAGAAGGCA CATGGCTGAA TATCGACGGT TTCCATATGG GGATTGGTGG
            CTTCTTCCGT GTACCGACTT ATAGCTGGCA AAGGTATACC CCTAACCACC

+2            D  D  S   W  S  P  S   V  S  A   E  F  Q   L  S  A
            ----------------------------------------------------
4351        CGACGACTCC TGGAGCCCGT CAGTATCGGC GGAATTCCAG CTGAGCGCCG
            GCTGCTGAGG ACCTCGGGCA GTCATAGCCG CCTTAAGGTC GACTCGCGGC

+2          G  R  Y  H   Y  Q  L   V  W  C  Q   K  R  S   D  Y  K
            ----------------------------------------------------
4401        GTCGCTACCA TTACCAGTTG GTCTGGTGTC AAAAAAGATC TGACTATAAA
            CAGCGATGGT AATGGTCAAC CAGACCACAG TTTTTTCTAG ACTGATATTT

+2           D  E  D  L   D  H  H   H  H  H   H  R
            ------------------------------------->
4451        GATGAGGACC TCGACCATCA TCATCATCAT CACCGGTAAT AATAGGTAGA
            CTACTCCTGG AGCTGGTAGT AGTAGTAGTA GTGGCCATTA TTATCCATCT

4501        TAAGTGACTG ATTAGATGCA TTGATCCCTC GACCAATTCC GGTTATTTTC
            ATTCACTGAC TAATCTACGT AACTAGGGAG CTGGTTAAGG CCAATAAAAG

4551        CACCATATTG CCGTCTTTTG GCAATGTGAG GGCCCGGAAA CCTGGCCCTG
            GTGGTATAAC GGCAGAAAAC CGTTACACTC CCGGGCCTTT GGACCGGGAC
```

FIG.10B-11

pICAST ALC

```
4601    TCTTCTTGAC GAGCATTCCT AGGGGTCTTT CCCCTCTCGC CAAAGGAATG
        AGAAGAACTG CTCGTAAGGA TCCCCAGAAA GGGGAGAGCG GTTTCCTTAC

4651    CAAGGTCTGT TGAATGTCGT GAAGGAAGCA GTTCCTCTGG AAGCTTCTTG
        GTTCCAGACA ACTTACAGCA CTTCCTTCGT CAAGGAGACC TTCGAAGAAC

4701    AAGACAAACA ACGTCTGTAG CGACCCTTTG CAGGCAGCGG AACCCCCCAC
        TTCTGTTTGT TGCAGACATC GCTGGGAAAC GTCCGTCGCC TTGGGGGGTG

4751    CTGGCGACAG GTGCCTCTGC GGCCAAAAGC CACGTGTATA AGATACACCT
        GACCGCTGTC CACGGAGACG CCGGTTTTCG GTGCACATAT TCTATGTGGA

4801    GCAAAGGCGG CACAACCCCA GTGCCACGTT GTGAGTTGGA TAGTTGTGGA
        CGTTTCCGCC GTGTTGGGGT CACGGTGCAA CACTCAACCT ATCAACACCT

4851    AAGAGTCAAA TGGCTCTCCT CAAGCGTATT CAACAAGGGG CTGAAGGATG
        TTCTCAGTTT ACCGAGAGGA GTTCGCATAA GTTGTTCCCC GACTTCCTAC

4901    CCCAGAAGGT ACCCCATTGT ATGGGATCTG ATCTGGGGCC TCGGTGCACA
        GGGTCTTCCA TGGGGTAACA TACCCTAGAC TAGACCCCGG AGCCACGTGT

4951    TGCTTTACAT GTGTTTAGTC GAGGTTAAAA AACGTCTAGG CCCCCCGAAC
        ACGAAATGTA CACAAATCAG CTCCAATTTT TTGCAGATCC GGGGGGCTTG

5001    CACGGGGACG TGGTTTTCCT TTGAAAAACA CGATGATAAT ACCATGATTG

        GTGCCCCTGC ACCAAAAGGA AACTTTTTGT GCTACTATTA TGGTACTAAC

5051    AACAAGATGG ATTGCACGCA GGTTCTCCGG CCGCTTGGGT GGAGAGGCTA
        TTGTTCTACC TAACGTGCGT CCAAGAGGCC GGCGAACCCA CCTCTCCGAT

5101    TTCGGCTATG ACTGGGCACA ACAGACAATC GGCTGCTCTG ATGCCGCCGT
        AAGCCGATAC TGACCCGTGT TGTCTGTTAG CCGACGAGAC TACGGCGGCA

5151    GTTCCGGCTG TCAGCGCAGG GGCGCCCGGT TCTTTTTGTC AAGACCGACC
        CAAGGCCGAC AGTCGCGTCC CCGCGGGCCA AGAAAAACAG TTCTGGCTGG
```

FIG.10B-12

pICAST ALC

```
5201    TGTCCGGTGC CCTGAATGAA CTGCAGGACG AGGCAGCGCG GCTATCGTGG
        ACAGGCCACG GGACTTACTT GACGTCCTGC TCCGTCGCGC CGATAGCACC

5251    CTGGCCACGA CGGGCGTTCC TTGCGCAGCT GTGCTCGACG TTGTCACTGA
        GACCGGTGCT GCCCGCAAGG AACGCGTCGA CACGAGCTGC AACAGTGACT

5301    AGCGGGAAGG GACTGGCTGC TATTGGGCGA AGTGCCGGGG CAGGATCTCC
        TCGCCCTTCC CTGACCGACG ATAACCCGCT TCACGGCCCC GTCCTAGAGG

5351    TGTCATCTCA CCTTGCTCCT GCCGAGAAAG TATCCATCAT GGCTGATGCA
        ACAGTAGAGT GGAACGAGGA CGGCTCTTTC ATAGGTAGTA CCGACTACGT

5401    ATGCGGCGGC TGCATACGCT TGATCCGGCT ACCTGCCCAT TCGACCACCA
        TACGCCGCCG ACGTATGCGA ACTAGGCCGA TGGACGGGTA AGCTGGTGGT

5451    AGCGAAACAT CGCATCGAGC GAGCACGTAC TCGGATGGAA GCCGGTCTTG
        TCGCTTTGTA GCGTAGCTCG CTCGTGCATG AGCCTACCTT CGGCCAGAAC

5501    TCGATCAGGA TGATCTGGAC GAAGAGCATC AGGGGCTCGC GCCAGCCGAA
        AGCTAGTCCT ACTAGACCTG CTTCTCGTAG TCCCCGAGCG CGGTCGGCTT

5551    CTGTTCGCCA GGCTCAAGGC GCGCATGCCC GACGGCGAGG ATCTCGTCGT
        GACAAGCGGT CCGAGTTCCG CGCGTACGGG CTGCCGCTCC TAGAGCAGCA

5601    GACCCATGGC GATGCCTGCT TGCCGAATAT CATGGTGGAA AATGGCCGCT
        CTGGGTACCG CTACGGACGA ACGGCTTATA GTACCACCTT TTACCGGCGA

5651    TTTCTGGATT CATCGACTGT GGCCGGCTGG GTGTGGCGGA CCGCTATCAG
        AAAGACCTAA GTAGCTGACA CCGGCCGACC CACACCGCCT GGCGATAGTC

5701    GACATAGCGT TGGCTACCCG TGATATTGCT GAAGAGCTTG GCGGCGAATG
        CTGTATCGCA ACCGATGGGC ACTATAACGA CTTCTCGAAC CGCCGCTTAC

5751    GGCTGACCGC TTCCTCGTGC TTTACGGTAT CGCCGCTCCC GATTCGCAGC
        CCGACTGGCG AAGGAGCACG AAATGCCATA GCGGCGAGGG CTAAGCGTCG
```

FIG.10B-13

pICAST ALC

5801 GCATCGCCTT CTATCGCCTT CTTGACGAGT TCTTCTGAGC GGGACTCTGG
CGTAGCGGAA GATAGCGGAA GAACTGCTCA AGAAGACTCG CCCTGAGACC

5851 GGTTCGCATC GATAAAATAA AAGATTTTAT TTAGTCTCCA GAAAAAGGGG
CCAAGCGTAG CTATTTTATT TTCTAAAATA AATCAGAGGT CTTTTTCCCC

5901 GGAATGAAAG ACCCCACCTG TAGGTTTGGC AAGCTAGCTT AAGTAACGCC
CCTTACTTTC TGGGGTGGAC ATCCAAACCG TTCGATCGAA TTCATTGCGG

5951 ATTTTGCAAG GCATGGAAAA ATACATAACT GAGAATAGAG AAGTTCAGAT
TAAAACGTTC CGTACCTTTT TATGTATTGA CTCTTATCTC TTCAAGTCTA

6001 CAAGGTCAGG AACAGATGGA ACAGCTGAAT ATGGGCCAAA CAGGATATCT
GTTCCAGTCC TTGTCTACCT TGTCGACTTA TACCCGGTTT GTCCTATAGA

6051 GTGGTAAGCA GTTCCTGCCC CGGCTCAGGG CCAAGAACAG ATGGAACAGC
CACCATTCGT CAAGGACGGG GCCGAGTCCC GGTTCTTGTC TACCTTGTCG

6101 TGAATATGGG CCAAACAGGA TATCTGTGGT AAGCAGTTCC TGCCCCGGCT
ACTTATACCC GGTTTGTCCT ATAGACACCA TTCGTCAAGG ACGGGGCCGA

6151 CAGGGCCAAG AACAGATGGT CCCCAGATGC GGTCCAGCCC TCAGCAGTTT
GTCCCGGTTC TTGTCTACCA GGGGTCTACG CCAGGTCGGG AGTCGTCAAA

6201 CTAGAGAACC ATCAGATGTT TCCAGGGTGC CCCAAGGACC TGAAATGACC
GATCTCTTGG TAGTCTACAA AGGTCCCACG GGGTTCCTGG ACTTTACTGG

6251 CTGTGCCTTA TTTGAACTAA CCAATCAGTT CGCTTCTCGC TTCTGTTCGC
GACACGGAAT AAACTTGATT GGTTAGTCAA GCGAAGAGCG AAGACAAGCG

6301 GCGCTTCTGC TCCCCGAGCT CAATAAAAGA GCCCACAACC CCTCACTCGG
CGCGAAGACG AGGGGCTCGA GTTATTTTCT CGGGTGTTGG GGAGTGAGCC

6351 GGCGCCAGTC CTCCGATTGA CTGAGTCGCC CGGGTACCCG TGTATCCAAT
CCGCGGTCAG GAGGCTAACT GACTCAGCGG GCCCATGGGC ACATAGGTTA

FIG.10B-14

pICAST ALC

6401 AAACCCTCTT GCAGTTGCAT CCGACTTGTG GTCTCGCTGT TCCTTGGGAG
TTTGGGAGAA CGTCAACGTA GGCTGAACAC CAGAGCGACA AGGAACCCTC

6451 GGTCTCCTCT GAGTGATTGA CTACCCGTCA GCGGGGGTCT TTCATTCATG
CCAGAGGAGA CTCACTAACT GATGGGCAGT CGCCCCCAGA AAGTAAGTAC

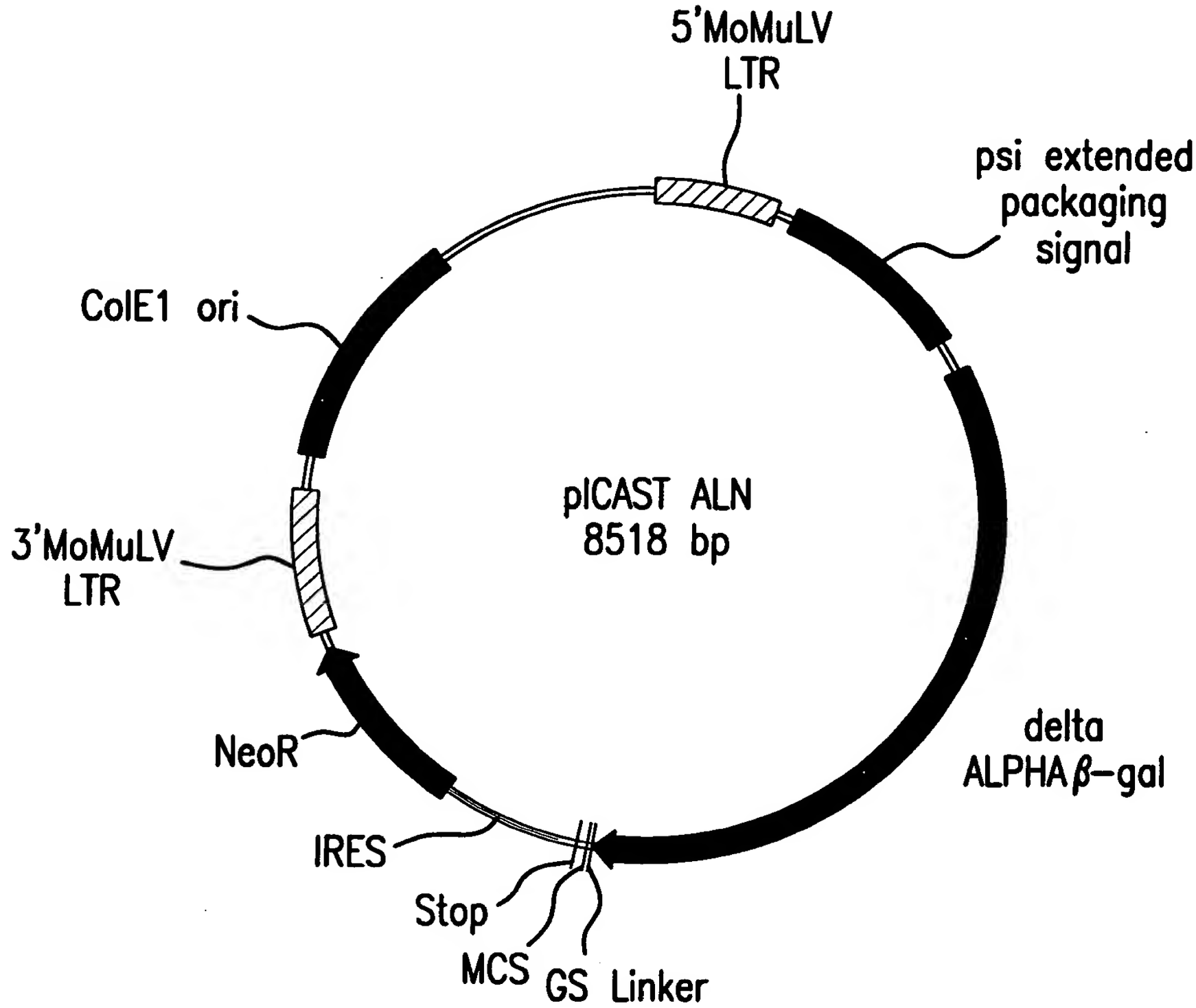
6501 CAGCATGTAT CAAAATTAAT TTGGTTTTTT TTCTTAAGTA TTTACATTAA
GTCGTACATA GTTTTAATTA AACCAAAAAA AAGAATTCAT AAATGTAATT

6551 ATGGCCATAG TTGCATTAAT GAATCGGCCA ACGCGCGGGG AGAGGCGGTT
TACCGGTATC AACGTAATTA CTTAGCCGGT TGCGCGCCCC TCTCCGCCAA

6601 TGCGTATTGG CGCTCTTCCG CTTCCTCGCT CACTGACTCG CTGCGCTCGG
ACGCATAACC GCGAGAAGGC GAAGGAGCGA GTGACTGAGC GACGCGAGCC

6651 TCGTTCGGCT GCGGCGAGCG GTATCAGCTC ACTCAAAGGC GGTAATACGG
AGCAAGCCGA CGCCGCTCGC CATAGTCGAG TGAGTTTCCG CCATTATGCC

FIG.10B-15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LTR
psi extended
packaging
signal
ColE1 ori
pICAST ALN
8518 bp
3'MoMuLV
LTR
delta
ALPHA β–gal
NeoR
IRES
Stop
MCS
GS Linker

FIG.11A

pICAST ALN

```
CTGCAGCCTG AATATGGGCC AAACAGGATA TCTGTGGTAA GCAGTTCCTG CCCCGGCTCA     60
GACGTCGGAC TTATACCCGG TTTGTCCTAT AGACACCATT CGTCAAGGAC GGGGCCGAGT     60

GGGCCAAGAA CAGATGGAAC AGCTGAATAT GGGCCAAACA GGATATCTGT GGTAAGCAGT    120
CCCGGTTCTT GTCTACCTTG TCGACTTATA CCCGGTTTGT CCTATAGACA CCATTCGTCA    120

TCCTGCCCCG GCTCAGGGCC AAGAACAGAT GGTCCCCAGA TGCGGTCCAG CCCTCAGCAG    180
AGGACGGGGC CGAGTCCCGG TTCTTGTCTA CCAGGGGTCT ACGCCAGGTC GGGAGTCGTC    180

TTTCTAGAGA ACCATCAGAT GTTTCCAGGG TGCCCCAAGG ACCTGAAATG ACCCTGTGCC    240
AAAGATCTCT TGGTAGTCTA CAAAGGTCCC ACGGGGTTCC TGGACTTTAC TGGGACACGG    240

TTATTTGAAC TAACCAATCA GTTCGCTTCT CGCTTCTGTT CGCGCGCTTC TGCTCCCCGA    300
AATAAACTTG ATTGGTTAGT CAAGCGAAGA GCGAAGACAA GCGCGCGAAG ACGAGGGGCT    300

GCTCAATAAA AGAGCCCACA ACCCGTCACT CGGGGCGCCA GTCCTCCGAT TGACTGAGTC    360
CGAGTTATTT TCTCGGGTGT TGGGGAGTGA GCCCCGCGGT CAGGAGGCTA ACTGACTCAG    360

GCCCGGGTAC CCGTGTATCC AATAAACCCT CTTGCAGTTG CATCCGACTT GTGGTCTCGC    420
CGGGCCCATG GGCACATAGG TTATTTGGGA GAACGTCAAC GTAGGCTGAA CACCAGAGCG    420

TGTTCCTTGG GAGGGTCTCC TCTGAGTGAT TGACTACCCG TCAGCGGGGG TCTTTCATTT    480
ACAAGGAACC CTCCCAGAGG AGACTCACTA ACTGATGGGC AGTCGCCCCC AGAAAGTAAA    480

GGGGGCTCGT CCGGGATCGG GAGACCCCTG CCCAGGGACC ACCGACCCAC CACCGGGAGG    540
CCCCCGAGCA GGCCCTAGCC CTCTGGGGAC GGGTCCCTGG TGGCTGGGTG GTGGCCCTCC    540

CAAGCTGGCC AGCAACTTAT CTGTGTCTGT CCGATTGTCT AGTGTCTATG ACTGATTTTA    600
GTTCGACCGG TCGTTGAATA GACACAGACA GGCTAACAGA TCACAGATAC TGACTAAAAT    600

TGCGCCTGCG TCGGTACTAG TTAGCTAACT AGCTCTGTAT CTGGCGGACC CGTGGTGGAA    660
ACGCGGACGC AGCCATGATC AATCGATTGA TCGAGACATA GACCGCCTGG GCACCACCTT    660

CTGACGAGTT CTGAACACCC GGCCGCAACC CTGGGAGACG TCCCAGGGAC TTTGGGGGCC    720
GACTGCTCAA GACTTGTGGG CCGGCGTTGG GACCCTCTGC AGGGTCCCTG AAACCCCCGG    720

GTTTTTGTGG CCCGACCTGA GGAAGGGAGT CGATGTGGAA TCCGACCCCG TCAGGATATG    780
CAAAAACACC GGGCTGGACT CCTTCCCTCA GCTACACCTT AGGCTGGGGC AGTCCTATAC    780
```

FIG.11B-1

pICAST ALN

```
TGGTTCTGGT AGGAGACGAG AACCTAAAAC AGTTCCCGCC TCCGTCTGAA TTTTTGCTTT    840
ACCAAGACCA TCCTCTGCTC TTGGATTTTG TCAAGGGCGG AGGCAGACTT AAAAACGAAA    840

CGGTTTGGAA CCGAAGCCGC GCGTCTTGTC TGCTGCAGCA TCGTTCTGTG TTGTCTCTGT    900
GCCAAACCTT GGCTTCGGCG CGCAGAACAG ACGACGTCGT AGCAAGACAC AACAGAGACA    900

CTGACTGTGT TTCTGTATTT GTCTGAAAAT TAGGGCCAGA CTGTTACCAC TCCCTTAAGT    960
GACTGACACA AAGACATAAA CAGACTTTTA ATCCCGGTCT GACAATGGTG AGGGAATTCA    960

TTGACCTTAG GTAACTGGAA AGATGTCGAG CGGCTCGCTC ACAACCAGTC GGTAGATGTC   1020
AACTGGAATC CATTGACCTT TCTACAGCTC GCCGAGCGAG TGTTGGTCAG CCATCTACAG   1020

AAGAAGAGAC GTTGGGTTAC CTTCTGCTCT GCAGAATGGC CAACCTTTAA CGTCGGATGG   1080
TTCTTCTCTG CAACCCAATG GAAGACGAGA CGTCTTACCG GTTGGAAATT GCAGCCTACC   1080

CCGCGAGACG GCACCTTTAA CCGAGACCTC ATCACCCAGG TTAAGATCAA GGTCTTTTCA   1140
GGCGCTCTGC CGTGGAAATT GGCTCTGGAG TAGTGGGTCC AATTCTAGTT CCAGAAAAGT   1140

CCTGGCCCGC ATGGACACCC AGACCAGGTC CCCTACATCG TGACCTGGGA AGCCTTGGCT   1200
GGACCGGGCG TACCTGTGGG TCTGGTCCAG GGGATGTAGC ACTGGACCCT TCGGAACCGA   1200

TTTGACCCCC CTCCCTGGGT CAAGCCCTTT GTACACCCTA AGCCTCCGCC TCCTCTTCCT   1260
AAACTGGGGG GAGGGACCCA GTTCGGGAAA CATGTGGGAT TCGGAGGCGG AGGAGAAGGA   1260

CCATCCGCCC CGTCTCTCCC CCTTGAACCT CCTCGTTCGA CCCCGCCTCG ATCCTCCCTT   1320
GGTAGGCGGG GCAGAGAGGG GGAACTTGGA GGAGCAAGCT GGGGCGGAGC TAGGAGGGAA   1320

TATCCAGCCC TCACTCCTTC TCTAGGCGCC GGCCGCTCTA GCCCATTAAT ACGACTCACT   1380
ATAGGTCGGG AGTGAGGAAG AGATCCGCGG CCGGCGAGAT CGGGTAATTA TGCTGAGTGA   1380

ATAGGGCGAT TCGAACACCA TGCACCATCA TCATCATCAC GTCGACTATA AAGATGAGGA   1440
TATCCCGCTA AGCTTGTGGT ACGTGGTAGT AGTAGTAGTG CAGCTGATAT TTCTACTCCT   1440

CCTCGAGATG GGCGTGATTA CGGATTCACT GGCCGTCGTG GCCCGCACCG ATCGCCCTTC   1500
GGAGCTCTAC CCGCACTAAT GCCTAAGTGA CCGGCAGCAC CGGGCGTGGC TAGCGGGAAG   1500

CCAACAGTTA CGCAGCCTGA ATGGCGAATG GCGCTTTGCC TGGTTTCCGG CACCAGAAGC   1560
GGTTGTCAAT GCGTCGGACT TACCGCTTAC CGCGAAACGG ACCAAAGGCC GTGGTCTTCG   1560
```

FIG.11B-2

pICAST ALN

```
GGTGCCGGAA AGCTGGCTGG AGTGCGATCT TCCTGAGGCC GATACTGTCG TCGTCCCCTC   1620
CCACGGCCTT TCGACCGACC TCACGCTAGA AGGACTCCGG CTATGACAGC AGCAGGGGAG   1620

AAACTGGCAG ATGCACGGTT ACGATGCGCC CATCTACACC AACGTGACCT ATCCCATTAC   1680
TTTGACCGTC TACGTGCCAA TGCTACGCGG GTAGATGTGG TTGCACTGGA TAGGGTAATG   1680

GGTCAATCCG CCGTTTGTTC CCACGGAGAA TCCGACGGGT TGTTACTCGC TCACATTTAA   1740
CCAGTTAGGC GGCAAACAAG GGTGCCTCTT AGGCTGCCCA ACAATGAGCG AGTGTAAATT   1740

TGTTGATGAA AGCTGGCTAC AGGAAGGCCA GACGCGAATT ATTTTTGATG GCGTTAACTC   1800
ACAACTACTT TCGACCGATG TCCTTCCGGT CTGCGCTTAA TAAAAACTAC CGCAATTGAG   1800

GGCGTTTCAT CTGTGGTGCA ACGGGCGCTG GGTCGGTTAC GGCCAGGACA GTCGTTTGCC   1860
CCGCAAAGTA GACACCACGT TGCCCGCGAC CCAGCCAATG CCGGTCCTGT CAGCAAACGG   1860

GTCTGAATTT GACCTGAGCG CATTTTTACG CGCCGGAGAA AACCGCCTCG CGGTGATGGT   1920
CAGACTTAAA CTGGACTCGC GTAAAAATGC GCGGCCTCTT TTGGCGGAGC GCCACTACCA   1920

GCTGGGCTGG AGTGACGGCA GTTATCTGGA AGATCAGGAT ATGTGGCGGA TGAGCGGCAT   1980
CGACGCGACC TCACTGCCGT CAATAGACCT TCTAGTCCTA TACACCGCCT ACTCGCCGTA   1980

TTTCCGTGAC GTCTCGTTGC TGCATAAACC GACTACACAA ATCAGCGATT TCCATGTTGC   2040
AAAGGCACTG CAGAGCAACG ACGTATTTGG CTGATGTGTT TAGTCGCTAA AGGTACAACG   2040

CACTCGCTTT AATGATGATT RCAGCCGCGC TGTACTGGAG GCTGAAGTTC AGATGTGCGG   2100
GTGAGCGAAA TTACTACTAA AGTCGGCGCG ACATGACCTC CGACTTCAAG TCTACACGCC   2100

CGAGTTGCGT GACTACCTAC GGGTAACAGT TTCTTTATGG CAGGGTGAAA CGCAGGTCGC   2160
GCTCAACGCA CTGATGGATG CCCATTGTCA AAGAAATACC GTCCCACTTT GCGTCCAGCG   2160

CAGCGGCACC GCGCCTTTCG GCGGTGAAAT TATCGATGAG CGTGGTGGTT ATGCCGATCG   2220
GTCGCCGTGG CGCGGAAAGC CGCCACTTTA ATAGCTACTC GCACCACCAA TACGGCTAGC   2220

CGTCACACTA CGTCTGAACG TCGAAAACCC GAAACTGTGG AGCGCCGAAA TCCCGAATCT   2280
GCAGTGTGAT GCAGACTTGC AGCTTTTGGG CTTTGACACC TCGCGGCTTT AGGGCTTAGA   2280

CTATCGTGCG GTGGTTGAAC TGCACACCGC CGACGGCACG CTGATTGAAG CAGAAGCCTG   2340
GATAGCACGC CACCAACTTG ACGTGTGGCG GCTGCCGTGC GACTAACTTC GTCTTCGGAC   2340
```

FIG.11B-3

```
CGATGTCGGT TTCCGCGAGG TGCGGATTGA AAATGGTCTG CTGCTGCTGA ACGGCAAGCC   2400
GCTACAGCCA AAGGCGCTCC ACGCCTAACT TTTACCAGAC GACGACGACT TGCCGTTCGG   2400

GTTGCTGATT CGAGGCGTTA ACCGTCACGA GCATCATCCT CTGCATGGTC AGGTCATGGA   2460
CAACGACTAA GCTCCGCAAT TGGCAGTGCT CGTAGTAGGA GACGTACCAG TCCAGTACCT   2460

TGAGCAGACG ATGGTGCAGG ATATCCTGCT GATGAAGCAG AACAACTTTA ACGCCGTGCG   2520
ACTCGTCTGC TACCACGTCC TATAGGACGA CTACTTCGTC TTGTTGAAAT TGCGGCACGC   2520

CTGTTCGCAT TATCCGAACC ATCCGCTGTG GTACACGCTG TGCGACCGCT ACGGCCTGTA   2580
GACAAGCGTA ATAGGCTTGG TAGGCGACAC CATGTGCGAC ACGCTGGCGA TGCCGGACAT   2580

TGTGGTGGAT GAAGCCAATA TTGAAACCCA CGGCATGGTG CCAATGAATC GTCTGACCGA   2640
ACACCACCTA CTTCGGTTAT AACTTTGGGT GCCGTACCAC GGTTACTTAG CAGACTGGCT   2640

TGATCCGCGC TGGCTACCGG CGATGAGCGA ACGCGTAACG CGAATGGTGC AGCGCGATCG   2700
ACTAGGCGCG ACCGATGGCC GCTACTCGCT TGCGCATTGC GCTTACCACG TCGCGCTAGC   2700

TAATCACCCG AGTGTGATCA TCTGGTCGCT GGGGAATGAA TCAGGCCACG GCGCTAATCA   2760
ATTAGTGGGC TCACACTAGT AGACCAGCGA CCCCTTACTT AGTCCGGTGC CGCGATTAGT   2760

CGACGCGCTG TATCGCTGGA TCAAATCTGT CGATCCTTCC CGCCCGGTGC AGTATGAAGG   2820
GCTGCGCGAC ATAGCGACCT AGTTTAGACA GCTAGGAAGG GCGGGCCACG TCATACTTCC   2820

CGGCGGAGCC GACACCACGG CCACCGATAT TATTTGCCCG ATGTACGCGC GCGTGGATGA   2880
GCCGCCTCGG CTGTGGTGCC GGTGGCTATA ATAAACGGGC TACATGCGCG CGCACCTACT   2880

AGACCAGCCC TTCCCGGCTG TGCCGAAATG GTCCATCAAA AAATGGCTTT CGCTACCTGG   2940
TCTGGTCGGG AAGGGCCGAC ACGGCTTTAC CAGGTAGTTT TTTACCGAAA GCGATGGACC   2940

AGAGACGCGC CCGCTGATCC TTTGCGAATA CGCCCACGCG ATGGGTAACA GTCTTGGCGG   3000
TCTCTGCGCG GGCGACTAGG AAACGCTTAT GCGGGTGCGC TACCCATTGT CAGAACCGCC   3000

TTTCGCTAAA TACTGGCAGG CGTTTCGTCA GTATCCCCGT TTACAGGGCG GCTTCGTCTG   3060
AAAGCGATTT ATGACCGTCC GCAAAGCAGT CATAGGGGCA AATGTCCCGC CGAAGCAGAC   3060

GGACTGGGTG GATCAGTCGC TGATTAAATA TGATGAAAAC GGCAACCCGT GGTCGGCTTA   3120
CCTGACCCAC CTAGTCAGCG ACTAATTTAT ACTACTTTTG CCGTTGGGCA CCAGCCGAAT   3120
```

FIG.11B-4

```
CGGCGGTGAT TTTGGCGATA CGCCGAACGA TCGCCAGTTC TGTATGAACG GTCTGGTCTT   3180
GCCGCCACTA AAACCGCTAT GCGGCTTGCT AGCGGTCAAG ACATACTTGC CAGACCAGAA   3180

TGCCGACCGC ACGCCGCATC CAGCGCTGAC GGAAGCAAAA CACCAGCAGC AGTTTTTCCA   3240
ACGGCTGGCG TGCGGCGTAG GTCGCGACTG CCTTCGTTTT GTGGTCGTCG TCAAAAAGGT   3240

GTTCCGTTTA TCCGGGCAAA CCATCGAAGT GACCAGCGAA TACCTGTTCC GTCATAGCGA   3300
CAAGGCAAAT AGGCCCGTTT GGTAGCTTCA CTGGTCGCTT ATGGACAAGG CAGTATCGCT   3300

TAACGAGCTC CTGCACTGGA TGGTGGCGCT GGATGGTAAG CCGCTGGCAA GCGGTGAAGT   3360
ATTGCTCGAG GACGTGACCT ACCACCGCGA CCTACCATTC GGCGACCGTT CGCCACTTCA   3360

GCCTCTGGAT GTCGCTCCAC AAGGTAAACA GTTGATTGAA CTGCCTGAAC TACCGCAGCC   3420
CGGAGACCTA CAGCGAGGTG TTCCATTTGT CAACTAACTT GACGGACTTG ATGGCGTCGG   3420

GGAGAGCGCC GGGCAACTCT GGCTCACAGT ACGCGTAGTG CAACCGAACG CGACCGCATG   3480
CCTCTCGCGG CCCGTTGAGA CCGAGTGTCA TGCGCATCAC GTTGGCTTGC GCTGGCGTAC   3480

GTCAGAAGCC GGGCACATCA GCGCCTGGCA GCAGTGGCGT CTGGCGGAAA ACCTCAGTGT   3540
CAGTCTTCGG CCCGTGTAGT CGCGGACCGT CGTCACCGCA GACCGCCTTT TGGAGTCACA   3540

GACGCTCCCC GCCGCGTCCC ACGCCATCCC GCATCTGACC ACCAGCGAAA TGGATTTTTG   3600
CTGCGAGGGG CGGCGCAGGG TGCGGTAGGG CGTAGACTGG TGGTCGCTTT ACCTAAAAAC   3600

CATCGAGCTG GGTAATAAGC GTTGGCAATT TAACCGCCAG TCAGGCTTTC TTTCACAGAT   3660
GTAGCTCGAC CCATTATTCG CAACCGTTAA ATTGGCGGTC AGTCCGAAAG AAAGTGTCTA   3660

GTGGATTGGC GATAAAAAAC AACTGCTGAC GCCGCTGCGC GATCAGTTCA CCCGTGCACC   3720
CACCTAACCG CTATTTTTTG TTGACGACTG CGGCGACGCG CTAGTCAAGT GGGCACGTGG   3720

GCTGGATAAC GACATTGGCG TAAGTGAAGC GACCCGCATT GACCCTAACG CCTGGGTCGA   3780
CGACCTATTG CTGTAACCGC ATTCACTTCG CTGGGCGTAA CTGGGATTGC GGACCCAGCT   3780

ACGCTGGAAG GCGGCGGGCC ATTACCAGGC CGAAGCAGCG TTGTTGCAGT GCACGGCAGA   3840
TGCGACCTTC CGCCGCCCGG TAATGGTCCG GCTTCGTCGC AACAACGTCA CGTGCCGTCT   3840

TACACTTGCT GATGCGGTGC TGATTACGAC CGCTCACGCG TGGCAGCATC AGGGGAAAAC   3900
ATGTGAACGA CTACGCCACG ACTAATGCTG GCGAGTGCGC ACCGTCGTAG TCCCCTTTTG   3900
```

FIG. 11B-5

pICAST ALN

```
CTTATTTATC AGCCGGAAAA CCTACCGGAT TGATGGTAGT GGTCAAATGG CGATTACCGT   3960
GAATAAATAG TCGGCCTTTT GGATGGCCTA ACTACCATCA CCAGTTTACC GCTAATGGCA   3960

TGATGTTGAA GTGGCGAGCG ATACACCGCA TCCGGCGCGG ATTGGCCTGA ACTGCCAGCT   4020
ACTACAACTT CACCGCTCGC TATGTGGCGT AGGCCGCGCC TAACCGGACT TGACGGTCGA   4020

GGCGCAGGTA GCAGAGCGGG TAAACTGGCT CGGATTAGGG CCGCAAGAAA ACTATCCCGA   4080
CCGCGTCCAT CGTCTCGCCC ATTTGACCGA GCCTAATCCC GGCGTTCTTT TGATAGGGCT   4080

CCGCCTTACT GCCGCCTGTT TTGACCGCTG GGATCTGCCA TTGTCAGACA TGTATACCCC   4140
GGCGGAATGA CGGCGGACAA AACTGGCGAC CCTAGACGGT AACAGTCTGT ACATATGGGG   4140

GTACGTCTTC CCGAGCGAAA ACGGTCTGCG CTGCGGGACG CGCGAATTGA ATTATGGCCC   4200
CATGCAGAAG GGCTCGCTTT TGCCAGACGC GACGCCCTGC GCGCTTAACT TAATACCGGG   4200

ACACCAGTGG CGCGGCGACT TCCAGTTCAA CATCAGCCGC TACAGTCAAC AGCAACTGAT   4260
TGTGGTCACC GCGCCGCTGA AGGTCAAGTT GTAGTCGGCG ATGTCAGTTG TCGTTGACTA   4260

GGAAACCAGC CATCGCCATC TGCTGCACGC GGAAGAAGGC ACATGGCTGA ATATCGACGG   4320
CCTTTGGTCG GTAGCGGTAG ACGACGTGCG CCTTCTTCCG TGTACCGACT TATAGCTGCC   4320

TTTCCATATG GGGATTGGTG GCGACGACTC CTGGAGCCCG TCAGTATCGG CGGAATTCCA   4380
AAAGGTATAC CCCTAACCAC CGCTGCTGAG GACCTCGGGC AGTCATAGCC GCCTTAAGGT   4380

GCTGAGCGCC GGTCGCTACC ATTACCAGTT GGTCTGGTGT CAAAAAAGAT CTGGAGGTGG   4440
CGACTCGCGG CCAGCGATGG TAATGGTCAA CCAGACCACA GTTTTTTCTA GACCTCCACC   4440

TGGCAGCAGG CCTTGGCGCG CCGGATCCTT AATTAACAAT TGACCGGTAA TAATAGGTAG   4500
ACCGTCGTCC GGAACCGCGC GGCCTAGGAA TTAATTGTTA ACTGGCCATT ATTATCCATC   4500

ATAAGTGACT GATTAGATGC ATTGATCCCT CGACCAATTC CGGTTATTTT CCACCATATT   4560
TATTCACTGA CTAATCTACG TAACTAGGGA GCTGGTTAAG GCCAATAAAA GGTGGTATAA   4560

GCCGTCTTTT GGCAATGTGA GGGCCCGGAA ACCTGGCCCT GTCTTCTTGA CGAGCATTCC   4620
CGGCAGAAAA CCGTTACACT CCCGGGCCTT TGGACCGGGA CAGAAGAACT GCTCGTAAGG   4620

TAGGGGTCTT TCCCCTCTCG CCAAAGGAAT GCAAGGTCTG TTGAATGTCG TGAAGGAAGC   4680
ATCCCCAGAA AGGGGAGAGC GGTTTCCTTA CGTTCCAGAC AACTTACAGC ACTTCCTTCG   4680
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FIG.11B-6

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AGTTCCTCTG GAAGCTTCTT GAAGACAAAC AACGTCTGTA GCGACCCTTT GCAGGCAGCG   4740
TCAAGGAGAC CTTCGAAGAA CTTCTGTTTG TTGCAGACAT CGCTGGGAAA CGTCCGTCGC   4740

GAACCCCCCA CCTGGCGACA GGTGCCTCTG CGGCCAAAAG CCACGTGTAT AAGATACACC   4800
CTTGGGGGGT GGACCGCTGT CCACGGAGAC GCCGGTTTTC GGTGCACATA TTCTATGTGG   4800

TGCAAAGGCG GCACAACCCC AGTGCCACGT TGTGAGTTGG ATAGTTGTGG AAAGAGTCAA   4860
ACGTTTCCGC CGTGTTGGGG TCACGGTGCA ACACTCAACC TATCAACACC TTTCTCAGTT   4860

ATGGCTCTCC TCAAGCGTAT TCAACAAGGG GCTGAAGGAT GCCCAGAAGG TACCCCATTG   4920
TACCGAGAGG AGTTCGCATA AGTTGTTCCC CGACTTCCTA CGGGTCTTCC ATGGGGTAAC   4920

TATGGGATCT GATCTGGGGC CTCGGTGCAC ATGCTTTACA TGTGTTTAGT CGAGGTTAAA   4980
ATACCCTAGA CTAGACCCCG GAGCCACGTG TACGAAATGT ACACAAATCA GCTCCAATTT   4980

AAACGTCTAG GCCCCCCGAA CCACGGGGAC GTGGTTTTCC TTTGAAAAAC ACGATGATAA   5040
TTTGCAGATC CGGGGGGCTT GGTGCCCCTG CACCAAAAGG AAACTTTTTG TGCTACTATT   5040

TACCATGATT GAACAAGATG GATTGCACGC AGGTTCTCCG GCCGCTTGGG TGGAGAGGCT   5100
ATGGTACTAA CTTGTTCTAC CTAACGTGCG TCCAAGAGGC CGGCGAACCC ACCTCTCCGA   5100

ATTCGGCTAT GACTGGGCAC AACAGACAAT CGGCTGCTCT GATGCCGCCG TGTTCCGGCT   5160
TAAGCCGATA CTGACCCGTG TTGTCTGTTA GCCGACGAGA CTACGGCGGC ACAAGGCCGA   5160

GTCAGCGCAG GGGCGCCCGG TTCTTTTTGT CAAGACCGAC CTGTCCGGTG CCCTGAATGA   5220
CAGTCGCGTC CCCGCGGGCC AAGAAAAACA GTTCTGGCTG GACAGGCCAC GGGACTTACT   5220

ACTGCAGGAC GAGGCAGCGC GGCTATCGTG GCTGGCCACG ACGGGCGTTC CTTGCGCAGC   5280
TGACGTCCTG CTCCGTCGCG CCGATAGCAC CGACCGGTGC TGCCCGCAAG GAACGCGTCG   5280

TGTGCTCGAC GTTGTCACTG AAGCGGGAAG GGACTGGCTG CTATTGGGCG AAGTGCCGGG   5340
ACACGAGCTG CAACAGTGAC TTCGCCCTTC CCTGACCGAC GATAACCCGC TTCACGGCCC   5340

GCAGGATCTC CTGTCATCTC ACCTTGCTCC TGCCGAGAAA GTATCCATCA TGGCTGATGC   5400
CGTCCTAGAG GACAGTAGAG TGGAACGAGG ACGGCTCTTT CATAGGTAGT ACCGACTACG   5400

AATGCGGCGG CTGCATACGC TTGATCCGGC TACCTGCCCA TTCGACCACC AAGCGAAACA   5460
TTACGCCGCC GACGTATGCG AACTAGGCCG ATGGACGGGT AAGCTGGTGG TTCGCTTTGT   5460
```


FIG.11B-7

```
TCGCATCGAG CGAGCACGTA CTCGGATGGA AGCCGGTCTT GTCGATCAGG ATGATCTGGA   5520
AGCGTAGCTC GCTCGTGCAT GAGCCTACCT TCGGCCAGAA CAGCTAGTCC TACTAGACCT   5520

CGAAGAGCAT CAGGGGCTCG CGCCAGCCGA ACTGTTCGCC AGGCTCAAGG CGCGCATGCC   5580
GCTTCTCGTA GTCCCCGAGC GCGGTCGGCT TGACAAGCGG TCCGAGTTCC GCGCGTACGG   5580

CGACGGCGAG GATCTCGTCG TGACCCATGG CGATGCCTGC TTGCCGAATA TCATGGTGGA   5640
GCTGCCGCTC CTAGAGCAGC ACTGGGTACC GCTACGGACG AACGGCTTAT AGTACCACCT   5640

AAATGGCCGC TTTTCTGGAT TCATCGACTG TGGCCGGCTG GGTGTGGCGG ACCGCTATCA   5700
TTTACCGGCG AAAAGACCTA AGTAGCTGAC ACCGGCCGAC CCACACCGCC TGGCGATAGT   5700

GGACATAGCG TTGGCTACCC GTGATATTGC TGAAGAGCTT GGCGGCGAAT GGGCTGACCG   5760
CCTGTATCGC AACCGATGGG CACTATAACG ACTTCTCGAA CCGCCGCTTA CCCGACTGGC   5760

CTTCCTCGTG CTTTACGGTA TCGCCGCTCC CGATTCGCAG CGCATCGCCT TCTATCGCCT   5820
GAAGGAGCAC GAAATGCCAT AGCGGCGAGG GCTAAGCGTC GCGTAGCGGA AGATAGCGGA   5820

TCTTGACGAG TTCTTCTGAG CGGGACTCTG GGGTTCGCAT CGATAAAATA AAAGATTTTA   5880
AGAACTGCTC AAGAAGACTC GCCCTGAGAC CCCAAGCGTA GCTATTTTAT TTTCTAAAAT   5880

TTTAGTCTCC AGAAAAAGGG GGGAATGAAA GACCCCACCT GTAGGTTTGG CAAGCTAGCT   5940
AAATCAGAGG TCTTTTTCCC CCCTTACTTT CTGGGGTGGA CATCCAAACC GTTCGATCGA   5940

TAAGTAACGC CATTTTGCAA GGCATGGAAA AATACATAAC TGAGAATAGA GAAGTTCAGA   6000
ATTCATTGCG GTAAAACGTT CCGTACCTTT TTATGTATTG ACTCTTATCT CTTCAAGTCT   6000

TCAAGGTCAG GAACAGATGG AACAGCTGAA TATGGGCCAA ACAGGATATC TGTGGTAAGC   6060
AGTTCCAGTC CTTGTCTACC TTGTCGACTT ATACCCGGTT TGTCCTATAG ACACCATTCG   6060

AGTTCCTGCC CCGGCTCAGG GCCAAGAACA GATGGAACAG CTGAATATGG GCCAAACAGG   6120
TCAAGGACGG GGCCGAGTCC CGGTTCTTGT CTACCTTGTC GACTTATACC CGGTTTGTCC   6120

ATATCTGTGG TAAGCAGTTC CTGCCCCGGC TCAGGGCCAA GAACAGATGG TCCCCAGATG   6180
TATAGACACC ATTCGTCAAG GACGGGGCCG AGTCCCGGTT CTTGTCTACC AGGGGTCTAC   6180

CGGTCCAGCC CTCAGCAGTT TCTAGAGAAC CATCAGATGT TTCCAGGGTG CCCCAAGGAC   6240
GCCAGGTCGG GAGTCGTCAA AGATCTCTTG GTAGTCTACA AAGGTCCCAC GGGGTTCCTG   6240
```

FIG.11B-8

```
CTGAAATGAC CCTGTGCCTT ATTTGAACTA ACCAATCAGT TCGCTTCTCG CTTCTGTTCG   6300
GACTTTACTG GGACACGGAA TAAACTTGAT TGGTTAGTCA AGCGAAGAGC GAAGACAAGC   6300

CGCGCTTCTG CTCCCCGAGC TCAATAAAAG AGCCCACAAC CCCTCACTCG GGGCGCCAGT   6360
GCGCGAAGAC GAGGGGCTCG AGTTATTTTC TCGGGTGTTG GGGAGTGAGC CCCGCGGTCA   6360

CCTCCGATTG ACTGAGTCGC CCGGGTACCC GTGTATCCAA TAAACCCTCT TGCAGTTGCA   6420
GGAGGCTAAC TGACTCAGCG GGCCCATGGG CACATAGGTT ATTTGGGAGA ACGTCAACGT   6420

TCCGACTTGT GGTCTCGCTG TTCCTTGGGA GGGTCTCCTC TGAGTGATTG ACTACCCGTC   6480
AGGCTGAACA CCAGAGCGAC AAGGAACCCT CCCAGAGGAG ACTCACTAAC TGATGGGCAG   6480

AGCGGGGGTC TTTCATTCAT GCAGCATGTA TCAAAATTAA TTTGGTTTTT TTTCTTAAGT   6540
TCGCCCCCAG AAAGTAAGTA CGTCGTACAT AGTTTTAATT AAACCAAAAA AAAGAATTCA   6540

ATTTACATTA AATGGCCATA GTTGCATTAA TGAATCGGCC AACGCGCGGG GAGAGGCGGT   6600
TAAATGTAAT TTACCGGTAT CAACGTAATT ACTTAGCCGG TTGCGCGCCC CTCTCCGCCA   6600

AACGCATAAC CGCGAGAAGG CGAAGGAGCG AGTGACTGAG CGACGCGAGC CAGCAAGCCG   6660
TTGCGTATTG GCGCTCTTCC GCTTCCTCGC TCACTGACTC GCTGCGCTCG GTCGTTCGGC   6660

TGCGGCGAGC GGTATCAGCT CACTCAAAGG CGGTAATACG GTTATCCACA GAATCAGGGG   6720
ACGCCGCTCG CCATAGTCGA GTGAGTTTCC GCCATTATGC CAATAGGTGT CTTAGTCCCC   6720

ATAACGCAGG AAAGAACATG TGAGCAAAAG GCCAGCAAAA GGCCAGGAAC CGTAAAAAGG   6780
TATTGCGTCC TTTCTTGTAC ACTCGTTTTC CGGTCGTTTT CCGGTCCTTG GCATTTTTCC   6780

CCGCGTTGCT GGCGTTTTTC CATAGGCTCC GCCCCCCTGA CGAGCATCAC AAAAATCGAC   6840
GGCGCAACGA CCGCAAAAAG GTATCCGAGG CGGGGGGACT GCTCGTAGTG TTTTTAGCTG   6840

GCTCAAGTCA GAGGTGGCGA AACCCGACAG GACTATAAAG ATACCAGGCG TTTCCCCCTG   6900
CGAGTTCAGT CTCCACCGCT TTGGGCTGTC CTGATATTTC TATGGTCCGC AAAGGGGGAC   6900

GAAGCTCCCT CGTGCGCTCT CCTGTTCCGA CCCTGCCGCT TACCGGATAC CTGTCCGCCT   6960
CTTCGAGGGA GCACGCGAGA GGACAAGGCT GGGACGGCGA ATGGCCTATG GACAGGCGGA   6960

TTCTCCCTTC GGGAAGCGTG GCGCTTTCTC ATAGCTCACG CTGTAGGTAT CTCAGTTCGG   7020
AAGAGGGAAG CCCTTCGCAC CGCGAAAGAG TATCGAGTGC GACATCCATA GAGTCAAGCC   7020
```


FIG.11B-9

```
TGTAGGTCGT TCGCTCCAAG CTGGGCTGTG TGCACGAACC CCCCGTTCAG CCCGACCGCT   7080
ACATCCAGCA AGCGAGGTTC GACCCGACAC ACGTGCTTGG GGGGCAAGTC GGGCTGGCGA   7080

GCGCCTTATC CGGTAACTAT CGTCTTGAGT CCAACCCGGT AAGACACGAC TTATCGCCAC   7140
CGCGGAATAG GCCATTGATA GCAGAACTCA GGTTGGGCCA TTCTGTGCTG AATAGCGGTG   7140

TGGCAGCAGC CACTGGTAAC AGGATTAGCA GAGCGAGGTA TGTAGGCGGT GCTACAGAGT   7200
ACCGTCGTCG GTGACCATTG TCCTAATCGT CTCGCTCCAT ACATCCGCCA CGATGTCTCA   7200

TCTTGAAGTG GTGGCCTAAC TACGGCTACA CTAGAAGAAC AGTATTTGGT ATCTGCGCTC   7260
AGAACTTCAC CACCGGATTG ATGCCGATGT GATCTTCTTG TCATAAACCA TAGACGCGAG   7260

TGCTGAAGCC AGTTACCTTC GGAAAAAGAG TTGGTAGCTC TTGATCCGGC AAACAAACCA   7320
ACGACTTCGG TCAATGGAAG CCTTTTTCTC AACCATCGAG AACTAGGCCG TTTGTTTGGT   7320

CCGCTGGTAG CGGTGGTTTT TTTGTTTGCA AGCAGCAGAT TACGCGCAGA AAAAAAGGAT   7380
GGCGACCATC GCCACCAAAA AAACAAACGT TCGTCGTCTA ATGCGCGTCT TTTTTTCCTA   7380

CTCAAGAAGA TCCTTTGATC TTTTCTACGG GGTCTGACGC TCAGTGGAAC GAAAACTCAC   7440
GAGTTCTTCT AGGAAACTAG AAAAGATGCC CCAGACTGCG AGTCACCTTG CTTTTGAGTG   7440

GTTAAGGGAT TTTGGTCATG AGATTATCAA AAAGGATCTT CACCTAGATC CTTTTGCGGC   7500
CAATTCCCTA AAACCAGTAC TCTAATAGTT TTTCCTAGAA GTGGATCTAG GAAAACGCCG   7500

CGCAAATCAA TCTAAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTTACCA ATGCTTAATC   7560
GCGTTTAGTT AGATTTCATA TATACTCATT TGAACCAGAC TGTCAATGGT TACGAATTAG   7560

AGTGAGGCAC CTATCTCAGC GATCTGTCTA TTTCGTTCAT CCATAGTTGC CTGACTCCCC   7620
TCACTCCGTG GATAGAGTCG CTAGACAGAT AAAGCAAGTA GGTATCAACG GACTGAGGGG   7620

GTCGTGTAGA TAACTACGAT ACGGGAGGGC TTACCATCTG GCCCCAGTGC TGCAATGATA   7680
CAGCACATCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC CGGGGTCACG ACGTTACTAT   7680

CCGCGAGACC CACGCTCACC GGCTCCAGAT TTATCAGCAA TAAACCAGCC AGCCGGAAGG   7740
GGCGCTCTGG GTGCGAGTGG CCGAGGTCTA AATAGTCGTT ATTTGGTCGG TCGGCCTTCC   7740

GCCGAGCGCA GAAGTGGTCC TGCAACTTTA TCCGCCTCCA TCCAGTCTAT TAATTGTTGC   7800
CGGCTCGCGT CTTCACCAGG ACGTTGAAAT AGGCGGAGGT AGGTCAGATA ATTAACAACG   7800
```


FIG.11B-10

pICAST ALN

```
CGGGAAGCTA GAGTAAGTAG TTCGCCAGTT AATAGTTTGC GCAACGTTGT TGCCATTGCT   7860
GCCCTTCGAT CTCATTCATC AAGCGGTCAA TTATCAAACG CGTTGCAACA ACGGTAACGA   7860

ACAGGCATCG TGGTGTCACG CTCGTCGTTT GGTATGGCTT CATTCAGCTC CGGTTCCCAA   7920
TGTCCGTAGC ACCACAGTGC GAGCAGCAAA CCATACCGAA GTAAGTCGAG GCCAAGGGTT   7920

CGATCAAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA AAGCGGTTAG CTCCTTCGGT   7980
GCTAGTTCCG CTCAATGTAC TAGGGGGTAC AACACGTTTT TTCGCCAATC GAGGAAGCCA   7980

CCTCCGATCG TTGTCAGAAG TAAGTTGGCC GCAGTGTTAT CACTCATGGT TATGGCAGCA   8040
GGAGGCTAGC AACAGTCTTC ATTCAACCGG CGTCACAATA GTGAGTACCA ATACCGTCGT   8040

CTGCATAATT CTCTTACTGT CATGCCATCC GTAAGATGCT TTTCTGTGAC TGGTGAGTAC   8100
GACGTATTAA GAGAATGACA GTACGGTAGG CATTCTACGA AAAGACACTG ACCACTCATG   8100

TCAACCAAGT CATTCTGAGA ATAGTGTATG CGGCGACCGA GTTGCTCTTG CCCGGCGTCA   8160
AGTTGGTTCA GTAAGACTCT TATCACATAC GCCGCTGGCT CAACGAGAAC GGGCCGCAGT   8160

ATACGGGATA ATACCGCGCC ACATAGCAGA ACTTTAAAAG TGCTCATCAT TGGAAAACGT   8220
TATGCCCTAT TATGGCGCGG TGTATCGTCT TGAAATTTTC ACGAGTAGTA ACCTTTTGCA   8220

TCTTCGGGGC GAAAACTCTC AAGGATCTTA CCGCTGTTGA GATCCAGTTC GATGTAACCC   8280
AGAAGCCCCG CTTTTGAGAG TTCCTAGAAT GGCGACAACT CTAGGTCAAG CTACATTGGG   8280

ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA CCAGCGTTTC TGGGTGAGCA   8340
TGAGCACGTG GGTTGACTAG AAGTCGTAGA AAATGAAAGT GGTCGCAAAG ACCCACTCGT   8340

AAAACAGGAA GGCAAAATGC CGCAAAAAAG GGAATAAGGG CGACACGGAA ATGTTGAATA   8400
TTTTGTCCTT CCGTTTTACG GCGTTTTTTC CCTTATTCCC GCTGTGCCTT TACAACTTAT   8400

CTCATACTCT TCCTTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC   8460
GAGTATGAGA AGGAAAAAGT TATAATAACT TCGTAAATAG TCCCAATAAC AGAGTACTCG   8460

GGATACATAT TTGAATGTAT TTAGAAAAAT AAACAAATAG GGGTTCCGCG CACATTTC     8518
CCTATGTATA AACTTACATA AATCTTTTTA TTTGTTTATC CCCAAGGCGC GTGTAAAG     8518
```

FIG.11B-11

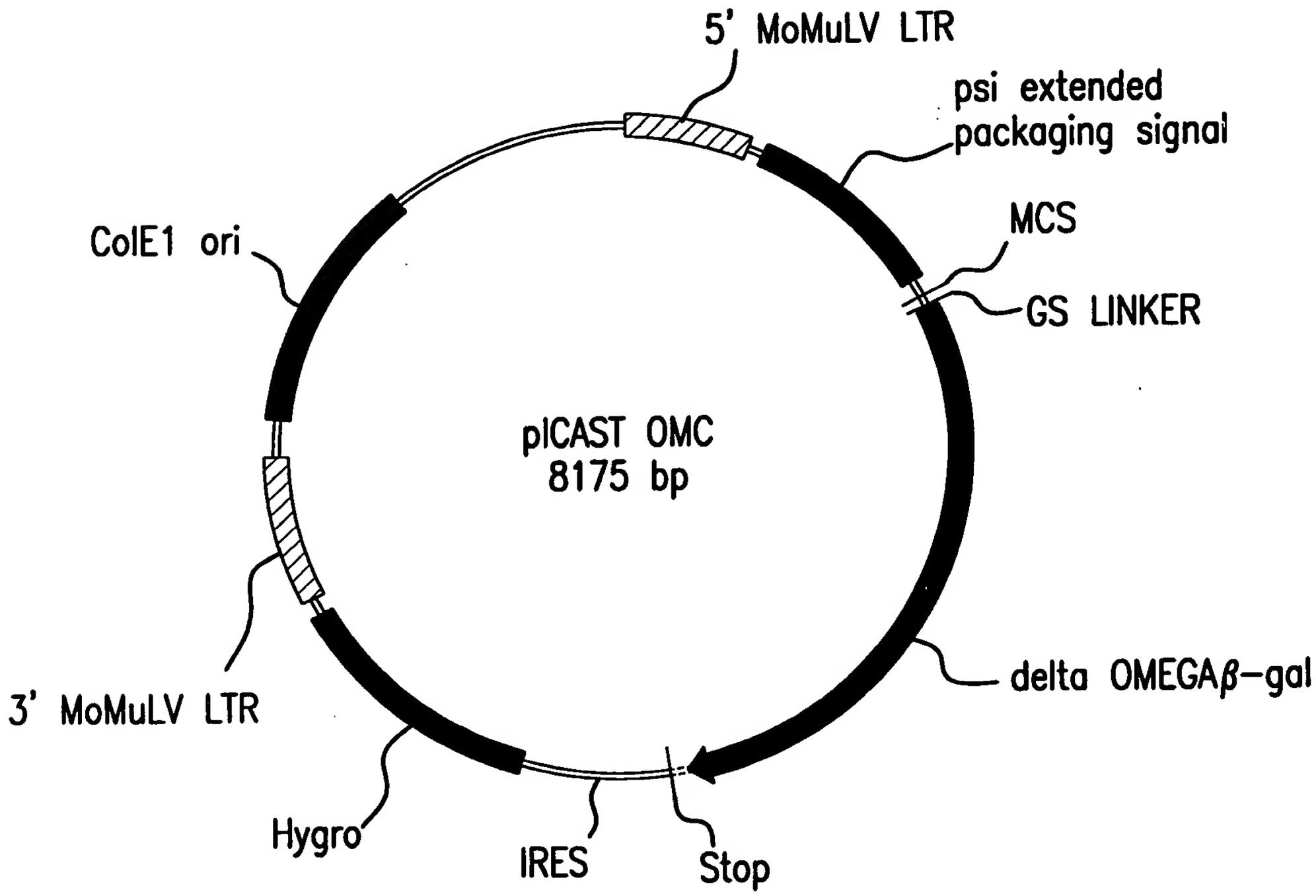

FIG.12A

pICAST OMC

```
CTGCAGCCTG AATATGGGCC AAACAGGATA TCTGTGGTAA GCAGTTCCTG CCCCGGCTCA     60
GACGTCGGAC TTATACCCGG TTTGTCCTAT AGACACCATT CGTCAAGGAC GGGGCCGAGT     60

GGGCCAAGAA CAGATGGAAC AGCTGAATAT GGGCCAAACA GGATATCTGT GGTAAGCAGT    120
CCCGGTTCTT GTCTACCTTG TCGACTTATA CCCGGTTTGT CCTATAGACA CCATTCGTCA    120

TCCTGCCCCG GCTCAGGGCC AAGAACAGAT GGTCCCCAGA TGCGGTCCAG CCCTCAGCAG    180
AGGACGGGGC CGAGTCCCGG TTCTTGTCTA CCAGGGGTCT ACGCCAGGTC GGGAGTCGTC    180

TTTCTAGAGA ACCATCAGAT GTTTCCAGGG TGCCCCAAGG ACCTGAAATG ACCCTGTGCC    240
AAAGATCTCT TGGTAGTCTA CAAAGGTCCC ACGGGGTTCC TGGACTTTAC TGGGACACGG    240

TTATTTGAAC TAACCAATCA GTTCGCTTCT CGCTTCTGTT CGCGCGCTTC TGCTCCCCGA    300
AATAAACTTG ATTGGTTAGT CAAGCGAAGA GCGAAGACAA GCGCGCGAAG ACGAGGGGCT    300

GCTCAATAAA AGAGCCCACA ACCCCTCACT CGGGGCGCCA GTCCTCCGAT TGACTGAGTC    360
CGAGTTATTT TCTCGGGTGT TGGGGAGTGA GCCCCGCGGT CAGGAGGCTA ACTGACTCAG    360

GCCCGGGTAC CCGTGTATCC AATAAACCCT CTTGCAGTTG CATCCGACTT GTGGTCTCGC    420
CGGGCCCATG GGCACATAGG TTATTTGGGA GAACGTCAAC GTAGGCTGAA CACCAGAGCG    420

TGTTCCTTGG GAGGYTCTCC TCTGAGTGAT TGACTACCCG TCAGCGGGGG TCTTTCATTT    480
ACAAGGAACC CTCCCAGAGG AGACTCACTA ACTGATGGGC AGTCGCCCCC AGAAAGTAAA    480

GGGGGCTCGT CCGGGATCGG GAGACCCCTG CCCAGGGACC ACCGACCCAC CACCGGGAGG    540
CCCCCGAGCA GGCCCTAGCC CTCTGGGGAC GGGTCCCTGG TGGCTGGGTG GTGGCCCTCC    540

CAAGCTGGCC AGCAACTTAT CTGTGTCTGT CCGATTGTCT AGTGTCTATG ACTGATTTTA    600
GTTCGACCGG TCGTTGAATA GACACAGACA GGCTAACAGA TCACAGATAC TGACTAAAAT    600

TGCGCCTGCG TCGGTACTAG TTAGCTAACT AGCTCTGTAT CTGGCGGACC CGTGGTGGAA    660
ACGCGGACGC AGCCATGATC AATCGATTGA TCGAGACATA GACCGCCTGG GCACCACCTT    660

CTGACGAGTT CTGAACACCC GGCCGCAACC CTGGGAGACG TCCCAGGGAC TTTGGGGGCC    720
GACTGCTCAA GACTTGTGGG CCGGCGTTGG GACCCTCTGC AGGGTCCCTG AAACCCCCGG    720

GTTTTTGTGG CCCGACCTGA GGAAGGGAGT CGATGTGGAA TCCGACCCCG TCAGGATATG    780
CAAAAACACC GGGCTGGACT CCTTCCCTCA GCTACACCTT AGGCTGGGGC AGTCCTATAC    780
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FIG.12B-1

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TGGTTCTGGT AGGAGACGAG AACCTAAAAC AGTTCCCGCC TCCGTCTGAA TTTTTGCTTT    840
ACCAAGACCA TCCTCTGCTC TTGGATTTTG TCAAGGGCGG AGGCAGACTT AAAAACGAAA    840

CGGTTTGGAA CCGAAGCCGC GCGTCTTGTC TGCTGCAGCA TCGTTCTGTG TTGTCTCTGT    900
GCCAAACCTT GGCTTCGGCG CGCAGAACAG ACGACGTCGT AGCAAGACAC AACAGAGACA    900

CTGACTGTGT TTCTGTATTT GTCTGAAAAT TAGGGCCAGA CTGTTACCAC TCCCTTAAGT    960
GACTGACACA AAGACATAAA CAGACTTTTA ATCCCGGTCT GACAATGGTG AGGGAATTCA    960

TTGACCTTAG GTAACTGGAA AGATGTCGAG CGGCTCGCTC ACAACCAGTC GGTAGATGTC   1020
AACTGGAATC CATTGACCTT TCTACAGCTC GCCGAGCGAG TGTTGGTCAG CCATCTACAG   1020

AAGAAGAGAC GTTGGGTTAC CTTCTGCTCT GCAGAATGGC CAACCTTTAA CGTCGGATGG   1080
TTCTTCTCTG CAACCCAATG GAAGACGAGA CGTCTTACCG GTTGGAAATT GCAGCCTACC   1080

CCGCGAGACG GCACCTTTAA CCGAGACCTC ATCACCCAGG TTAAGATCAA GGTCTTTTCA   1140
GGCGCTCTGC CGTGGAAATT GGCTCTGGAG TAGTGGGTCC AATTCTAGTT CCAGAAAAGT   1140

CCTGGCCCGC ATGGACACCC AGACCAGGTC CCCTACATCG TGACCTGGGA AGCCTTGGCT   1200
GGACCGGGCG TACCTGTGGG TCTGGTCCAG GGGATGTAGC ACTGGACCCT TCGGAACCGA   1200

TTTGACCCCC CTCCCTGGGT CAAGCCCTTT GTACACCCTA AGCCTCCGCC TCCTCTTCCT   1260
AAACTGGGGG GAGGGACCCA GTTCGGGAAA CATGTGGGAT TCGGAGGCGG AGGAGAAGGA   1260

CCATCCGCCC CGTCTCTCCC CCTTGAACCT CCTCGTTCGA CCCCGCCTCG ATCCTCCCTT   1320
GGTAGGCGGG GCAGAGAGGG GGAACTTGGA GGAGCAAGCT GGGGCGGAGC TAGGAGGGAA   1320

TATCCAGCCC TCACTCCTTC TCTAGGCGCC GGCCGCTCTA GCCCATTAAT ACGACTCACT   1380
ATAGGTCGGG AGTGAGGAAG AGATCCGCGG CCGGCGAGAT CGGGTAATTA TGCTGAGTGA   1380

ATAGGGCGAT TCGAATCAGG CCTTGGCGCG CCGGATCCTT AATTAAGCGC AATTGGGAGG   1440
TATCCCGCTA AGCTTAGTCC GGAACCGCGC GGCCTAGGAA TTAATTCGCG TTAACCCTCC   1440

TGGCGGTAGC CTCGAGATGG GCGTGATTAC GGATTCACTG GCCGTCGTTT TACAACGTCG   1500
ACCGCCATCG GAGCTCTACC CGCACTAATG CCTAAGTGAC CGGCAGCAAA ATGTTGCAGC   1500

TGACTGGGAA AACCCTGGCG TTACCCAACT TAATCGCCTT GCAGCACATC CCCCTTTCGC   1560
ACTGACCCTT TTGGGACCGC AATGGGTTGA ATTAGCGGAA CGTCGTGTAG GGGGAAAGCG   1560
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FIG.12B-2

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CAGCTGGCGT AATAGCGAAG AGGCCCGCAC CGATCGCCCT TCCCAACAGT TACGCAGCCT   1620
GTCGACCGCA TTATCGCTTC TCCGGGCGTG GCTAGCGGGA AGGGTTGTCA ATGCGTCGGA   1620

GAATGGCGAA TGGCGCTTTG CCTGGTTTCC GGCACCAGAA GCGGTGCCGG AAAGCTGGCT   1680
CTTACCGCTT ACCGCGAAAC GGACCAAAGG CCGTGGTCTT CGCCACGGCC TTTCGACCGA   1680

GGAGTGCGAT CTTCCTGAGG CCGATACTGT CGTCGTCCCC TCAAACTGGC AGATGCACGG   1740
CCTCACGCTA GAAGGACTCC GGCTATGACA GCAGCAGGGG AGTTTGACCG TCTACGTGCC   1740

TTACGATGCG CCCATCTACA CCAACGTGAC CTATCCCATT ACGGTCAATC CGCCGTTTGT   1800
AATGCTACGC GGGTAGATGT GGTTGCACTG GATAGGGTAA TGCCAGTTAG GCGGCAAACA   1800

TCCCACGGAG AATCCGACGG GTTGTTACTC GCTCACATTT AATGTTGATG AAAGCTGGCT   1860
AGGGTGCCTC TTAGGCTGCC CAACAATGAG CGAGTGTAAA TTACAACTAC TTTCGACCGA   1860

ACAGGAAGGC CAGACGCGAA TTATTTTTGA TGGCGTTAAC TCGGCGTTTC ATCTGTGGTG   1920
TGTCCTTCCG GTCTGCGCTT AATAAAAACT ACCGCAATTG AGCCGCAAAG TAGACACCAC   1920

CAACGGGCGC TGGGTCGGTT ACGGCCAGGA CAGTCGTTTG CCGTCTGAAT TTGACCTGAG   1980
GTTGCCCGCG ACCCAGCCAA TGCCGGTCCT GTCAGCAAAC GGCAGACTTA AACTGGACTC   1980

CGCATTTTTA CGCGCCGGAG AAAACCGCCT CGCGGTGATG GTGCTGCGCT GGAGTGACGG   2040
GCGTAAAAAT GCGCGGCCTC TTTTGGCGGA GCGCCACTAC CACGACGCGA CCTCACTGCC   2040

CAGTTATCTG GAAGATCAGG ATATGTGGCG GATGAGCGGC ATTTTCCGTG ACGTCTCGTT   2100
GTCAATAGAC CTTCTAGTCC TATACACCGC CTACTCGCCG TAAAAGGCAC TGCAGAGCAA   2100

GCTGCATAAA CCGACTACAC AAATCAGCGA TTTCCATGTT GCCACTCGCT TTAATGATGA   2160
CGACGTATTT GGCTGATGTG TTTAGTCGCT AAAGGTACAA CGGTGAGCGA AATTACTACT   2160

TTTCAGCCGC GCTGTACTGG AGGCTGAAGT TCAGATGTGC GGCGAGTTGC GTGACTACCT   2220
AAAGTCGGCG CGACATGACC TCCGACTTCA AGTCTACACG CCGCTCAACG CACTGATGGA   2220

ACGGGTAACA GTTTCTTTAT GGCAGGGTGA AACGCAGGTC GCCAGCGGCA CCGCGCCTTT   2280
TGCCCATTGT CAAAGAAATA CCGTCCCACT TTGCGTCCAG CGGTCGCCGT GGCGCGGAAA   2280

CGGCGGTGAA ATTATCGATG AGCGTGGTGG TTATGCCGAT CGCGTCACAC TACGTCTGAA   2340
GCCGCCACTT TAATAGCTAC TCGCACCACC AATACGGCTA GCGCAGTGTG ATGCAGACTT   2340
```

FIG.12B-3

pICAST OMC

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CGTCGAAAAC CCGAAACTGT GGAGCGCCGA AATCCCGAAT CTCTATCGTG CGGTGGTTGA   2400
GCAGCTTTTG GGCTTTGACA CCTCGCGGCT TTAGGGCTTA GAGATAGCAC GCCACCAACT   2400

ACTGCACACC GCCGACGGCA CGCTGATTGA AGCAGAAGCC TGCGATGTCG GTTTCCGCGA   2460
TGACGTGTGG CGGCTGCCGT GCGACTAACT TCGTCTTCGG ACGCTACAGC CAAAGGCGCT   2460

GGTGCGGATT GAAAATGGTC TGCTGCTGCT GAACGGCAAG CCGTTGCTGA TTCGAGGCGT   2520
CCACGCCTAA CTTTTACCAG ACGACGACGA CTTGCCGTTC GGCAACGACT AAGCTCCGCA   2520

TAACCGTCAC GAGCATCATC CTCTGCATGG TCAGGTCATG GATGAGCAGA CGATGGTGCA   2580
ATTGGCAGTG CTCGTAGTAG GAGACGTACC AGTCCAGTAC CTACTCGTCT GCTACCACGT   2580

GGATATCCTG CTGATGAAGC AGAACAACTT TAACGCCGTG CGCTGTTCGC ATTATCCGAA   2640
CCTATAGGAC GACTACTTCG TCTTGTTGAA ATTGCGGCAC GCGACAAGCG TAATAGGCTT   2640

CCATCCGCTG TGGTACACGC TGTGCGACCG CTACGGCCTG TATGTGGTGG ATGAAGCCAA   2700
GGTAGGCGAC ACCATGTGCG ACACGCTGGC GATGCCGGAC ATACACCACC TACTTCGGTT   2700

TATTGAAACC CACGGCATGG TGCCAATGAA TCGTCTGACC GATGATCCGC GCTGGCTACC   2760
ATAACTTTGG GTGCCGTACC ACGGTTACTT AGCAGACTGG CTACTAGGCG CGACCGATGG   2760

GGCGATGAGC GAACGCGTAA CGCGAATGGT GCAGCGCGAT CGTAATCACC CGAGTGTGAT   2820
CCGCTACTCG CTTGCGCATT GCGCTTACCA CGTCGCGCTA GCATTAGTGG GCTCACACTA   2820

CATCTGGTCG CTGGGGAATG AATCAGGCCA CGGCGCTAAT CACGACGCGC TGTATCGCTG   2880
GTAGACCAGC GACCCCTTAC TTAGTCCGGT GCCGCGATTA GTGCTGCGCG ACATAGCGAC   2880

GATCAAATCT GTCGATCCTT CCCGCCCGGT GCAGTATGAA GGCGGCGGAG CCGACACCAC   2940
CTAGTTTAGA CAGCTAGGAA GGGCGGGCCA CGTCATACTT CCGCCGCCTC GGCTGTGGTG   2940

GGCCACCGAT ATTATTTGCC CGATGTACGC GCGCGTGGAT GAAGACCAGC CCTTCCCGGC   3000
CCGGTGGCTA TAATAAACGG GCTACATGCG CGCGCACCTA CTTCTGGTCG GGAAGGGCCG   3000

TGTGCCGAAA TGGTCCATCA AAAAATGGCT TTCGCTACCT GGAGAGACGC GCCCGCTGAT   3060
ACACGGCTTT ACCAGGTAGT TTTTTACCGA AAGCGATGGA CCTCTCTGCG CGGGCGACTA   3060

CCTTTGCGAA TACGCCCACG CGATGGGTAA CAGTCTTGGC GGTTTCGCTA AATACTGGCA   3120
GGAAACGCTT ATGCGGGTGC GCTACCCATT GTCAGAACCG CCAAAGCGAT TTATGACCGT   3120
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FIG.12B-4

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GGCGTTTCGT CAGTATCCCC GTTTACAGGG CGGCTTCGTC TGGGACTGGG TGGATCAGTC   3180
CCGCAAAGCA GTCATAGGGG CAAATGTCCC GCCGAAGCAG ACCCTGACCC ACCTAGTCAG   3180

GCTGATTAAA TATGATGAAA ACGGCAACCC GTGGTCGGCT TACGGCGGTG ATTTTGGCGA   3240
CGACTAATTT ATACTACTTT TGCCGTTGGG CACCAGCCGA ATGCCGCCAC TAAAACCGCT   3240

TACGCCGAAC GATCGCCAGT TCTGTATGAA CGGTCTGGTC TTTGCCGACC GCACGCCGCA   3300
ATGCGGCTTG CTAGCGGTCA AGACATACTT GCCAGACCAG AAACGGCTGG CGTGCGGCGT   3300

TCCAGCGCTG ACGGAAGCAA AACACCAGCA GCAGTTTTTC CAGTTCCGTT TATCCGGGCA   3360
AGGTCGCGAC TGCCTTCGTT TTGTGGTCGT CGTCAAAAAG GTCAAGGCAA ATAGGCCCGT   3360

AACCATCGAA GTGACCAGCG AATACCTGTT CCGTCATAGC GATAACGAGC TCCTGCACTG   3420
TTGGTAGCTT CACTGGTCGC TTATGGACAA GGCAGTATCG CTATTGCTCG AGGACGTGAC   3420

GATGGTGGCG CTGGATGGTA AGCCGCTGGC AAGCGGTGAA GTGCCTCTGG ATGTCGCTCC   3480
CTACCACCGC GACCTACCAT TCGGCGACCG TTCGCCACTT CACGGAGACC TACAGCGAGG   3480

ACAAGGTAAA CAGTTGATTG AACTGCCTGA ACTACCGCAG CCGGAGAGCG CCGGGCAACT   3540
TGTTCCATTT GTCAACTAAC TTGACGGACT TGATGGCGTC GGCCTCTCGC GGCCCGTTGA   3540

CTGGCTCACA GTACGCGTAG TGCAACCGAA CGCGACCGCA TGGTCAGAAG CCGGGCACAT   3600
GACCGAGTGT CATGCGCATC ACGTTGGCTT GCGCTGGCGT ACCAGTCTTC GGCCCGTGTA   3600

CAGCGCCTGG CAGCAGTGGC GTCTGGCGGA AAACCTCAGT GTGACGCTCC CCGCCGCGTC   3660
GTCGCGGACC GTCGTCACCG CAGACCGCCT TTTGGAGTCA CACTGCGAGG GGCGGCGCAG   3660

CCACGCCATC CCGCATCTGA CCACCAGCGA AATGGATTTT TGCATCGAGC TGGGTAATAA   3720
GGTGCGGTAG GGCGTAGACT GGTGGTCGCT TTACCTAAAA ACGTAGCTCG ACCCATTATT   3720

GCGTTGGCAA TTTAACCGCC AGTCAGGCTT TCTTTCACAG ATGTGGATTG GCGATAAAAA   3780
CGCAACCGTT AAATTGGCGG TCAGTCCGAA AGAAAGTGTC TACACCTAAC CGCTATTTTT   3780

ACAACTGCTG ACGCCGCTGC GCGATCAGTT CACCCGTGTC GATAGATCTG AACAGAAACT   3840
TGTTGACGAC TGCGGCGACG CGCTAGTCAA GTGGGCACAG CTATCTAGAC TTGTCTTTGA   3840

CATTTCCGAA GAAGACCTAG TCGACCATCA TCATCATCAT CACCGGTAAT AATAGGTAGA   3900
GTAAAGGCTT CTTCTGGATC AGCTGGTAGT AGTAGTAGTA GTGGCCATTA TTATCCATCT   3900
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FIG.12B-5

pICAST OMC

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TAAGTGACTG ATTAGATGCA TTTCGACTAG ATCCCTCGAC CAATTCCGGT TATTTTCCAC   3960
ATTCACTGAC TAATCTACGT AAAGCTGATC TAGGGAGCTG GTTAAGGCCA ATAAAAGGTG   3960

CATATTGCCG TCTTTTGGCA ATGTGAGGGC CCGGAAACCT GGCCCTGTCT TCTTGACGAG   4020
GTATAACGGC AGAAAACCGT TACACTCCCG GGCCTTTGGA CCGGGACAGA AGAACTGCTC   4020

CATTCCTAGG GGTCTTTCCC CTCTCGCCAA AGGAATGCAA GGTCTGTTGA ATGTCGTGAA   4080
GTAAGGATCC CCAGAAAGGG GAGAGCGGTT TCCTTACGTT CCAGACAACT TACAGCACTT   4080

GGAAGCAGTT CCTCTGGAAG CTTCTTGAAG ACAAACAACG TCTGTAGCGA CCCTTTGCAG   4140
CCTTCGTCAA GGAGACCTTC GAAGAACTTC TGTTTGTTGC AGACATCGCT GGGAAACGTC   4140

GCAGCGGAAC CCCCCACCTG GCGACAGGTG CCTCTGCGGC CAAAAGCCAC GTGTATAAGA   4200
CGTCGCCTTG GGGGGTGGAC CGCTGTCCAC GGAGACGCCG GTTTTCGGTG CACATATTCT   4200

TACACCTGCA AAGGCGGCAC AACCCCAGTG CCACGTTGTG AGTTGGATAG TTGTGGAAAG   4260
ATGTGGACGT TTCCGCCGTG TTGGGGTCAC GGTGCAACAC TCAACCTATC AACACCTTTC   4260

AGTCAAATGG CTCTCCTCAA GCGTATTCAA CAAGGGGCTG AAGGATGCCC AGAAGGTACC   4320
TCAGTTTACC GAGAGGAGTT CGCATAAGTT GTTCCCCGAC TTCCTACGGG TCTTCCATGG   4320

CCATTGTATG GGATCTGATC TGGGGCCTCG GTGCACATGC TTTACATGTG TTTAGTCGAG   4380
GGTAACATAC CCTAGACTAG ACCCCGGAGC CACGTGTACG AAATGTACAC AAATCAGCTC   4380

GTTAAAAAAC GTCTAGGCCC CCCGAACCAC GGGGACGTGG TTTTCCTTTG AAAAACACGA   4440
CAATTTTTTG CAGATCCGGG GGGCTTGGTG CCCCTGCACC AAAAGGAAAC TTTTTGTGCT   4440

TGATAATACC ATGAAAAAGC CTGAACTCAC CGCGACGTCT GTCGAGAAGT TTCTGATCGA   4500
ACTATTATGG TACTTTTTCG GACTTGAGTG GCGCTGCAGA CAGCTCTTCA AAGACTAGCT   4500

AAAGTTCGAC AGCGTCTCCG ACCTGATGCA GCTCTCGGAG GGCGAAGAAT CTCGTGCTTT   4560
TTTCAAGCTG TCGCAGAGGC TGGACTACGT CGAGAGCCTC CCGCTTCTTA GAGCACGAAA   4560

CAGCTTCGAT GTAGGAGGGC GTGGATATGT CCTGCGGGTA AATAGCTGCG CCGATGGTTT   4620
GTCGAAGCTA CATCCTCCCG CACCTATACA GGACGCCCAT TTATCGACGC GGCTACCAAA   4620

CTACAAAGAT CGTTATGTTT ATCGGCACTT TGCATCGGCC GCGCTCCCGA TTCCGGAAGT   4680
GATGTTTCTA GCAATACAAA TAGCCGTGAA ACGTAGCCGG CGCGAGGGCT AAGGCCTTCA   4680
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FIG.12B-6

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GCTTGACATT GGGGAATTTA GCGAGAGCCT GACCTATTGC ATCTCCCGCC GTGCACAGGG   4740
CGAACTGTAA CCCCTTAAAT CGCRCTCGGA CTGGATAACG TAGAGGGCGG CACGTGTCCC   4740

TGTCACGTTG CAAGACCTGC CTGAAACCGA ACTGCCCGCT GTTCTGCAGC CGGTCGCGGA   4800
ACAGTGCAAC GTTCTGGACG GACTTTGGCT TGACGGGCGA CAAGACGTCG GCCAGCGCCT   4800

GGCCATGGAT GCGATCGCTG CGGCCGATCT TAGCCAGACG AGCGGGTTCG GCCCATTCGG   4860
CCGGTACCTA CGCTAGCGAC GCCGGCTAGA ATCGGTCTGC TCGCCCAAGC CGGGTAAGCC   4860

ACCGCAAGGA ATCGGTCAAT ACACTACATG GCGTGATTTC ATATGCGCGA TTGCTGATCC   4920
TGGCGTTCCT TAGCCAGTTA TGTGATGTAC CGCACTAAAG TATACGCGCT AACGACTAGG   4920

CCATGTGTAT CACTGGCAAA CTGTGATGGA CGACACCGTC AGTGCGTCCG TCGCGCAGGC   4980
GGTACACATA GTGACCGTTT GACACTACCT GCTGTGGCAG TCACGCAGGC AGCGCGTCCG   4980

TCTCGATGAG CTGATGCTTT GGGCCGAGGA CTGCCCCGAA GTCCGGCACC TCGTGCACGC   5040
AGAGCTACTC GACTACGAAA CCCGGCTCCT GACGGGGCTT CAGGCCGTGG AGCACGTGCG   5040

GGATTTCGGC TCCAACAATG TCCTGACGGA CAATGGCCGC ATAACAGCGG TCATTGACTG   5100
CCTAAAGCCG AGGTTGTTAC AGGACTGCCT GTTACCGGCG TATTGTCGCC AGTAACTGAC   5100

GAGCGAGGCG ATGTTCGGGG ATTCCCAATA CGAGGTCGCC AACATCTTCT TCTGGAGGCC   5160
CTCGCTCCGC TACAAGCCCC TAAGGGTTAT GCTCCAGCGG TTGTAGAAGA AGACCTCCGG   5160

GTGGTTGGCT TGTATGGAGC AGCAGACGCG CTACTTCGAG CGGAGGCATC CGGAGCTTGC   5220
CACCAACCGA ACATACCTCG TCGTCTGCGC GATGAAGCTC GCCTCCGTAG GCCTCGAACG   5220

AGGATCGCCG CGGCTCCGGG CGTATATGCT CCGCATTGGT CTTGACCAAC TCTATCAGAG   5280
TCCTAGCGGC GCCGAGGCCC GCATATACGA GGCGTAACCA GAACTGCTTG AGATAGTCTC   5280

CTTGGTTGAC GGCAATTTCG ATGATGCAGC TTGGGCGCAG GGTCGATGCG ACGCAATCGT   5340
GAACCAACTG CCGTTAAAGC TACTACGTCG AACCCGCGTC CCAGCTACGC TGCGTTAGCA   5340

CCGATCCGGA GCCGGGACTG TCGGGCGTAC ACAAATCGCC CGCAGAAGCG CGGCCGTCTG   5400
GGCTAGGCCT CGGCCCTGAC AGCCCGCATG TGTTTAGCGG GCGTCTTCGC GCCGGCAGAC   5400

GACCGATGGC TGTGTAGAAG TACTCGCCGA TAGTGGAAAC CGACGCCCCA GCACTCGTCC   5460
CTGGCTACCG ACACATCTTC ATGAGCGGCT ATCACCTTTG GCTGCGGGGT CGTGAGCAGG   5460
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FIG.12B-7

pICAST OMC

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GAGGGCAAAG GAATAGAGTA GATGCCGACC GGGATCTATC GATAAAATAA AAGATTTTAT   5520
CTCCCGTTTC CTTATCTCAT CTACGGCTGG CCCTAGATAG CTATTTTATT TTCTAAAATA   5520

TTAGTCTCCA GAAAAAGGGG GGAATGAAAG ACCCCACCTG TAGGTTTGGC AAGCTAGCTT   5580
AATCAGAGGT CTTTTTCCCC CCTTACTTTC TGGGGTGGAC ATCCAAACCG TTCGATCGAA   5580

AAGTAACGCC ATTTTGCAAG GCATGGAAAA ATACATAACT GAGAATAGAG AAGTTCAGAT   5640
TTCATTGCGG TAAAACGTTC CGTACCTTTT TATGTATTGA CTCTTATCTC TTCAAGTCTA   5640

CAAGGTCAGG AACAGATGGA ACAGCTGAAT ATGGGCCAAA CAGGATATCT GTGGTAAGCA   5700
GTTCCAGTCC TTGTCTACCT TGTCGACTTA TACCCGGTTT GTCCTATAGA CACCATTCGT   5700

GTTCCTGCCC CGGCTCAGGG CCAAGAACAG ATGGAACAGC TGAATATGGG CCAAACAGGA   5760
CAAGGACGGG GCCGAGTCCC GGTTCTTGTC TACCTTGTCG ACTTATACCC GGTTTGTCCT   5760

TATCTGTGGT AAGCAGTTCC TGCCCCGGCT CAGGGCCAAG AACAGATGGT CCCCAGATGC   5820
ATAGACACCA TTCGTCAAGG ACGGGGCCGA GTCCCGGTTC TTGTCTACCA GGGGTCTACG   5820

GGTCCAGCCC TCAGCAGTTT CTAGAGAACC ATCAGATGTT TCCAGGGTGC CCCAAGGACC   5880
CCAGGTCGGG AGTCGTCAAA GATCTCTTGG TAGTCTACAA AGGTCCCACG GGGTTCCTGG   5880

TGAAATGACC CTGTGCCTTA TTTGAACTAA CCAATCAGTT CGCTTCTCGC TTCTGTTCGC   5940
ACTTTACTGG GACACGGAAT AAACTTGATT GGTTAGTCAA GCGAAGAGCG AAGACAAGCG   5940

GCGCTTCTGC TCCCCGAGCT CAATAAAAGA GCCCACAACC CCTCACTCGG GGCGCCAGTC   6000
CGCGAAGACG AGGGGCTCGA GTTATTTTCT CGGGTGTTGG GGAGTGAGCC CCGCGGTCAG   6000

CTCCGATTGA CTGAGTCGCC CGGGTACCCG TGTATCCAAT AAACCCTCTT GCAGTTGCAT   6060
GAGGCTAACT GACTCAGCGG GCCCATGGGC ACATAGGTTA TTTGGGAGAA CGTCAACGTA   6060

CCGACTTGTG GTCTCGCTGT TCCTTGGGAG GGTCTCCTCT GAGTGATTGA CTACCCGTCA   6120
GGCTGAACAC CAGAGCGACA AGGAACCCTC CCAGAGGAGA CTCACTAACT GATGGGCAGT   6120

GCGGGGGTCT TTCATTCATG CAGCATGTAT CAAAATTAAT TTGGTTTTTT TTCTTAAGTA   6180
CGCCCCCAGA AAGTAAGTAC GTCGTACATA GTTTTAATTA AACCAAAAAA AAGAATTCAT   6180

TTTACATTAA ATGGCCATAG TTGCATTAAT GAATCGGCCA ACGCGCGGGG AGAGGCGGTT   6240
AAATGTAATT TACCGGTATC AACGTAATTA CTTAGCCGGT TGCGCGCCCC TCTCCGCCAA   6240
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FIG.12B-8

pICAST OMC

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TGCGTATTGG CGCTCTTCCG CTTCCTCGCT CACTGACTCG CTGCGCTCGG TCGTTCGGCT   6300
ACGCATAACC GCGAGAAGGC GAAGGAGCGA GTGACTGAGC GACGCGAGCC AGCAAGCCGA   6300

GCGGCGAGCG GTATCAGCTC ACTCAAAGGC GGTAATACGG TTATCCACAG AATCAGGGGA   6360
CGCCGCTCGC CATAGTCGAG TGAGTTTCCG CCATTATGCC AATAGGTGTC TTAGTCCCCT   6360

TAACGCAGGA AAGAACATGT GAGCAAAAGG CCAGCAAAAG GCCAGGAACC GTAAAAAGGC   6420
ATTGCGTCCT TTCTTGTACA CTCGTTTTCC GGTCGTTTTC CGGTCCTTGG CATTTTTCCG   6420

CGCGTTGCTG GCGTTTTTCC ATAGGCTCCG CCCCCCTGAC GAGCATCACA AAAATCGACG   6480
GCGCAACGAC CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTCGTAGTGT TTTTAGCTGC   6480

CTCAAGTCAG AGGTGGCGAA ACCCGACAGG ACTATAAAGA TACCAGGCGT TTCCCCCTGG   6540
GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTTCT ATGGTCCGCA AAGGGGGACC   6540

AAGCTCCCTC GTGCGCTCTC CTGTTCCGAC CCTGCCGCTT ACCGGATACC TGTCCGCCTT   6600
TTCGAGGGAG CACGCGAGAG GACAAGGCTG GGACGGCGAA TGGCCTATGG ACAGGCGGAA   6600

TCTCCCTTCG GGAAGCGTGG CGCTTTCTCA TAGCTCACGC TGTAGGTATC TCAGTTCGGT   6660
AGAGGGAAGC CCTTCGCACC GCGAAAGAGT ATCGAGTGCG ACATCCATAG AGTCAAGCCA   6660

GTAGGTCGTT CGCTCCAAGC TGGGCTGTGT GCACGAACCC CCCGTTCAGC CCGACCGCTG   6720
CATCCAGCAA GCGAGGTTCG ACCCGACACA CGTGCTTGGG GGGCAAGTCG GGCTGGCGAC   6720

CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT TATCGCCACT   6780
GCGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA ATAGCGGTGA   6780

GGCAGCAGCC ACTGGTAACA GGATTAGCAG AGCGAGGTAT GTAGGCGGTG CTACAGAGTT   6840
CCGTCGTCGG TGACCATTGT CCTAATCGTC TCGCTCCATA CATCCGCCAC GATGTCTCAA   6840

CTTGAAGTGG TGGCCTAACT ACGGCTACAC TAGAAGAACA GTATTTGGTA TCTGCGCTCT   6900
GAACTTCACC ACCGGATTGA TGCCGATGTG ATCTTCTTGT CATAAACCAT AGACGCGAGA   6900

GCTGAAGCCA GTTACCTTCG GAAAAAGAGT TGGTAGCTCT TGATCCGGCA AACAAACCAC   6960
CGACTTCGGT CAATGGAAGC CTTTTTCTCA ACCATCGAGA ACTAGGCCGT TTGTTTGGTG   6960

CGCTGGTAGC GGTGGTTTTT TTGTTTGCAA GCAGCAGATT ACGCGCAGAA AAAAAGGATC   7020
GCGACCATCG CCACCAAAAA AACAAACGTT CGTCGTCTAA TGCGCGTCTT TTTTTCCTAG   7020
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FIG.12B-9

TCAAGAAGAT CCTTTGATCT TTTCTACGGG GTCTGACGCT CAGTGGAACG AAAACTCACG 7080
AGTTCTTCTA GGAAACTAGA AAAGATGCCC CAGACTGCGA GTCACCTTGC TTTTGAGTGC 7080

TTAAGGGATT TTGGTCATGA GATTATCAAA AAGGATCTTC ACCTAGATCC TTTTAAATTA 7140
AATTCCCTAA AACCAGTACT CTAATAGTTT TTCCTAGAAG TGGATCTAGG AAAATTTAAT 7140

AAAATGAAGT TTGCGGCCGC AAATCAATCT AAAGTATATA TGAGTAAACT TGGTCTGACA 7200
TTTTACTTCA AACGCCGGCG TTTAGTTAGA TTTCATATAT ACTCATTTGA ACCAGACTGT 7200

GTTACCAATG CTTAATCAGT GAGGCACCTA TCTCAGCGAT CTGTCTATTT CGTTCATCCA 7260
CAATGGTTAC GAATTAGTCA CTCCGTGGAT AGAGTCGCTA GACAGATAAA GCAAGTAGGT 7260

TAGTTGCCTG ACTCCCCGTC GTGTAGATAA CTACGATACG GGAGGGCTTA CCATCTGGCC 7320
ATCAACGGAC TGAGGGGCAG CACATCTATT GATGCTATGC CCTCCCGAAT GGTAGACCGG 7320

CCAGTGCTGC AATGATACCG CGAGACCCAC GCTCACCGGC TCCAGATTTA TCAGCAATAA 7380
GGTCACGACG TTACTATGGC GCTCTGGGTG CGAGTGGCCG AGGTCTAAAT AGTCGTTATT 7380

ACCAGCCAGC CGGAAGGGCC GAGCGCAGAA GTGGTCCTGC AACTTTATCC GCCTCCATCC 7440
TGGTCGGTCG GCCTTCCCGG CTCGCGTCTT CACCAGGACG TTGAAATAGG CGGAGGTAGG 7440

AGTCTATTAA TTGTTGCCGG GAAGCTAGAG TAAGTAGTTC GCCAGTTAAT AGTTTGCGCA 7500
TCAGATAATT AACAACGGCC CTTCGATCTC ATTCATCAAG CGGTCAATTA TCAAACGCGT 7500

ACGTTGTTGC CATTGCTACA GGCATCGTGG TGTCACGCTC GTCGTTTGGT ATGGCTTCAT 7560
TGCAACAACG GTAACGATGT CCGTAGCACC ACAGTGCGAG CAGCAAACCA TACCGAAGTA 7560

TCAGCTCCGG TTCCCAACGA TCAAGGCGAG TTACATGATC CCCCATGTTG TGCAAAAAAG 7620
AGTCGAGGCC AAGGGTTGCT AGTTCCGCTC AATGTACTAG GGGGTACAAC ACGTTTTTTC 7620

CGGTTAGCTC CTTCGGTCCT CCGATCGTTG TCAGAAGTAA GTTGGCCGCA GTGTTATCAC 7680
GCCAATCGAG GAAGCCAGGA GGCTAGCAAC AGTCTTCATT CAACCGGCGT CACAATAGTG 7680

TCATGGTTAT GGCAGCACTG CATAATTCTC TTACTGTCAT GCCATCCGTA AGATGCTTTT 7740
AGTACCAATA CCGTCGTGAC GTATTAAGAG AATGACAGTA CGGTAGGCAT TCTACGAAAA 7740

CTGTGACTGG TGAGTACTCA ACCAAGTCAT TCTGAGAATA GTGTATGCGG CGACCGAGTT 7800
GACACTGACC ACTCATGAGT TGGTTCAGTA AGACTCTTAT CACATACGCC GCTGGCTCAA 7800

FIG.12B-10

pICAST OMC

```
GCTCTTGCCC GGCGTCAATA CGGGATAATA CCGCGCCACA TAGCAGAACT TTAAAAGTGC   7860
CGAGAACGGG CCGCAGTTAT GCCCTATTAT GGCGCGGTGT ATCGTCTTGA AATTTTCACG   7860

TCATCATTGG AAAACGTTCT TCGGGGCGAA AACTCTCAAG GATCTTACCG CTGTTGAGAT   7920
AGTAGTAACC TTTTGCAAGA AGCCCCGCTT TTGAGAGTTC CTAGAATGGC GACAACTCTA   7920

CCAGTTCGAT GTAACCCACT CGTGCACCCA ACTGATCTTC AGCATCTTTT ACTTTCACCA   7980
GGTCAAGCTA CATTGGGTGA GCACGTGGGT TGACTAGAAG TCGTAGAAAA TGAAAGTGGT   7980

GCGTTTCTGG GTGAGCAAAA ACAGGAAGGC AAAATGCCGC AAAAAAGGGA ATAAGGGCGA   8040
CGCAAAGACC CACTCGTTTT TGTCCTTCCG TTTTACGGCG TTTTTTCCCT TATTCCCGCT   8040

CACGGAAATG TTGAATACTC ATACTCTTCC TTTTTCAATA TTATTGAAGC ATTTATCAGG   8100
GTGCCTTTAC AACTTATGAG TATGAGAAGG AAAAAGTTAT AATAACTTCG TAAATAGTCC   8100

GTTATTGTCT CATGAGCGGA TACATATTTG AATGTATTTA GAAAAATAAA CAAATAGGGG   8160
CAATAACAGA GTACTCGCCT ATGTATAAAC TTACATAAAT CTTTTTATTT GTTTATCCCC   8160

TTCCGCGCAC ATTTC                                                    8175
AAGGCGCGTG TAAAG                                                    8175
```

FIG.12B-11

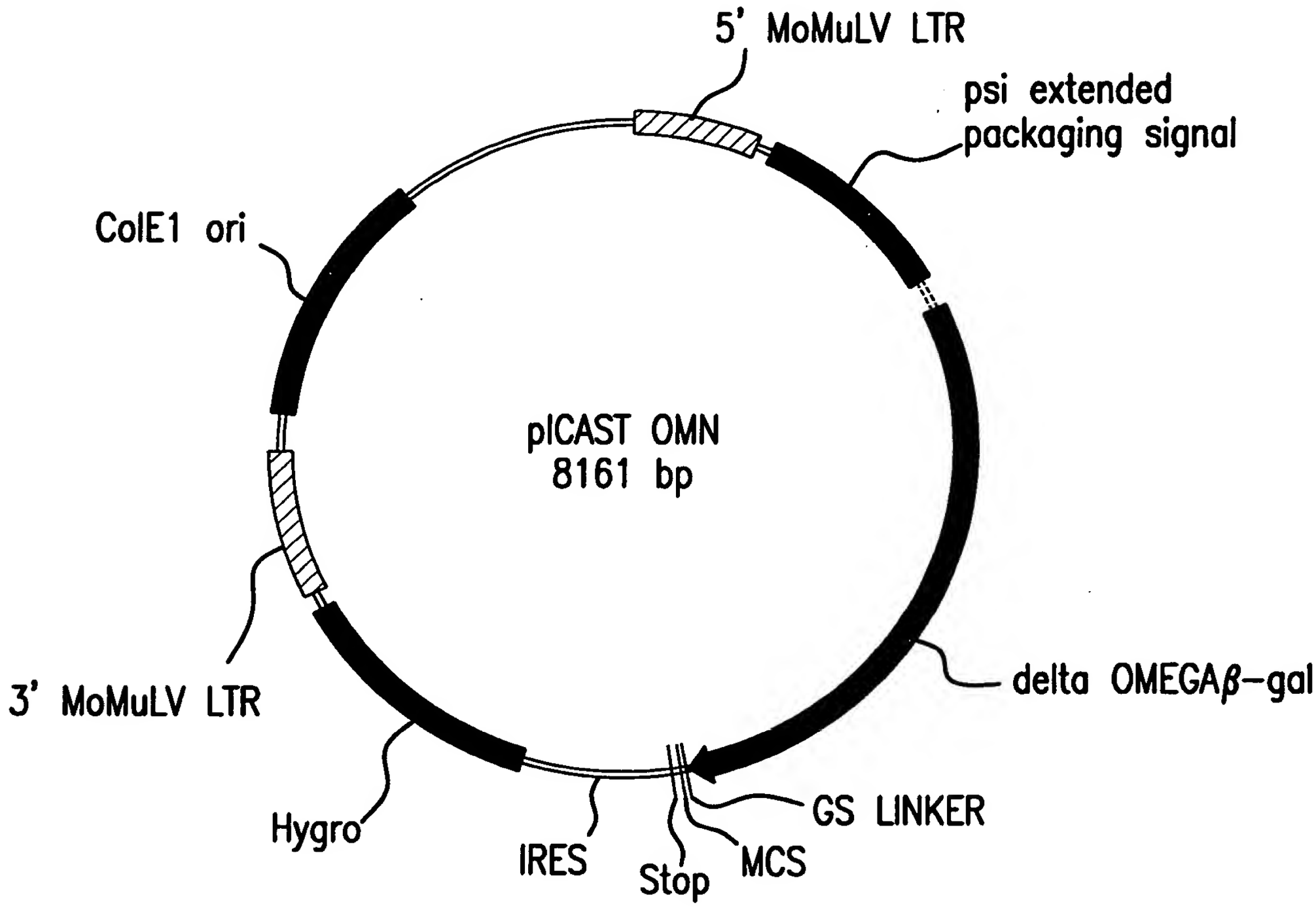

FIG.13A

pICAST OMN

```
CTGCAGCCTG AATATGGGCC AAACAGGATA TCTGTGGTAA GCAGTTCCTG CCCCGGCTCA      60
GACGTCGGAC TTATACCCGG TTTGTCCTAT AGACACCATT CGTCAAGGAC GGGGCCGAGT      60

GGGCCAAGAA CAGATGGAAC AGCTGAATAT GGGCCAAACA GGATATCTGT GGTAAGCAGT     120
CCCGGTTCTT GTCTACCTTG TCGACTTATA CCCGGTTTGT CCTATAGACA CCATTCGTCA     120

TCCTGCCCCG GCTCAGGGCC AAGAACAGAT GGTCCCCAGA TGCGGTCCAG CCCTCAGCAG     180
AGGACGGGGC CGAGTCCCGG TTCTTGTCTA CCAGGGGTCT ACGCCAGGTC GGGAGTCGTC     180

TTTCTAGAGA ACCATCAGAT GTTTCCAGGG TGCCCCAAGG ACCTGAAATG ACCCTGTGCC     240
AAAGATCTCT TGGTAGTCTA CAAAGGTCCC ACGGGGTTCC TGGACTTTAC TGGGACACGG     240

TTATTTGAAC TAACCAATCA GTTCGCTTCT CGCTTCTGTT CGCGCGCTTC TGCTCCCCGA     300
AATAAACTTG ATTGGTTAGT CAAGCGAAGA GCGAAGACAA GCGCGCGAAG ACGAGGGGCT     300

GCTCAATAAA AGAGCCCACA ACCCCTCACT CGGGGCGCCA GTCCTCCGAT TGACTGAGTC     360
CGAGTTATTT TCTCGGGTGT TGGGGAGTGA GCCCCGCGGT CAGGAGGCTA ACTGACTCAG     360

GCCCGGGTAC CCGTGTATCC AATAAACCCT CTTGCAGTTG CATCCGACTT GTGGTCTCGC     420
CGGGCCCATG GGCACATAGG TTATTTGGGA GAACGTCAAC GTAGGCTGAA CACCAGAGCG     420

TGTTCCTTGG GAGGGTCTCC TCTGAGTGAT TGACTACCCG TCAGCGGGGG TCTTTCATTT     480
ACAAGGAACC CTCCCAGAGG AGACTCACTA ACTGATGGGC AGTCGCCCCC AGAAAGTAAA     480

GGGGGCTCGT CCGGGATCGG GAGACCCCTG CCCAGGGACC ACCGACCCAC CACCGGGAGG     540
CCCCCGAGCA GGCCCTAGCC CTCTGGGGAC GGGTCCCTGG TGGCTGGGTG GTGGCCCTCC     540

CAAGCTGGCC AGCAACTTAT CTGTGTCTGT CCGATTGTCT AGTGTCTATG ACTGATTTTA     600
GTTCGACCGG TCGTTGAATA GACACAGACA GGCTAACAGA TCACAGATAC TGACTAAAAT     600

TGCGCCTGCG TCGGTACTAG TTAGCTAACT AGCTCTGTAT CTGGCGGACC CGTGGTGGAA     660
ACGCGGACGC AGCCATGATC AATCGATTGA TCGAGACATA GACCGCCTGG GCACCACCTT     660

CTGACGAGTT CTGAACACCC GGCCGCAACC CTGGGAGACG TCCCAGGGAC TTTGGGGGCC     720
GACTGCTCAA GACTTGTGGG CCGGCGTTGG GACCCTCTGC AGGGTCCCTG AAACCCCCGG     720

GTTTTTGTGG CCCGACCTGA GGAAGGGAGT CGATGTGGAA TCCGACCCCG TCAGGATATG     780
CAAAAACACC GGGCTGGACT CCTTCCCTCA GCTACACCTT AGGCTGGGGC AGTCCTATAC     780
```

FIG.13B-1

```
TGGTTCTGGT AGGAGACGAG AACCTAAAAC AGTTCCCGCC TCCGTCTGAA TTTTTGCTTT   840
ACCAAGACCA TCCTCTGCTC TTGGATTTTG TCAAGGGCGG AGGCAGACTT AAAAACGAAA   840

CGGTTTGGAA CCGAAGCCGC GCGTCTTGTC TGCTGCAGCA TCGTTCTGTG TTGTCTCTGT   900
GCCAAACCTT GGCTTCGGCG CGCAGAACAG ACGACGTCGT AGCAAGACAC AACAGAGACA   900

CTGACTGTGT TTCTGTATTT GTCTGAAAAT TAGGGCCAGA CTGTTACCAC TCCCTTAAGT   960
GACTGACACA AAGACATAAA CAGACTTTTA ATCCCGGTCT GACAATGGTG AGGGAATTCA   960

TTGACCTTAG GTAACTGGAA AGATGTCGAG CGGCTCGCTC ACAACCAGTC GGTAGATGTC  1020
AACTGGAATC CATTGACCTT TCTACAGCTC GCCGAGCGAG TGTTGGTCAG CCATCTACAG  1020

AAGAAGAGAC GTTGGGTTAC CTTCTGCTCT GCAGAATGGC CAACCTTTAA CGTCGGATGG  1080
TTCTTCTCTG CAACCCAATG GAAGACGAGA CGTCTTACCG GTTGGAAATT GCAGCCTACC  1080

CCGCGAGACG GCACCTTTAA CCGAGACCTC ATCACCCAGG TTAAGATCAA GGTCTTTTCA  1140
GGCGCTCTGC CGTGGAAATT GGCTCTGGAG TAGTGGGTCC AATTCTAGTT CCAGAAAAGT  1140

CCTGGCCCGC ATGGACACCC AGACCAGGTC CCCTACATCG TGACCTGGGA AGCCTTGGCT  1200
GGACCGGGCG TACCTGTGGG TCTGGTCCAG GGGATGTAGC ACTGGACCCT TCGGAACCGA  1200

TTTGACCCCC CTCCCTGGGT CAAGCCCTTT GTACACCCTA AGCCTCCGCC TCCTCTTCCT  1260
AAACTGGGGG GAGGGACCCA GTTCGGGAAA CATGTGGGAT TCGGAGGCGG AGGAGAAGGA  1260

CCATCCGCCC CGTCTCTCCC CCTTGAACCT CCTCGTTCGA CCCCGCCTCG ATCCTCCCTT  1320
GGTAGGCGGG GCAGAGAGGG GGAACTTGGA GGAGCAAGCT GGGGCGGAGC TAGGAGGGAA  1320

TATCCAGCCC TCACTCCTTC TCTAGGCGCC GGCCGCTCTA GCCCATTAAT ACGACTCACT  1380
ATAGGTCGGG AGTGAGGAAG AGATCCGCGG CCGGCGAGAT CGGGTAATTA TGCTGAGTGA  1380

ATAGGGCGAT TCGAACACCA TGCACCATCA TCATCATCAC GTCGACGAAC AGAAACTCAT  1440
TATCCCGCTA AGCTTGTGGT ACGTGGTAGT AGTAGTAGTG CAGCTGCTTG TCTTTGAGTA  1440

TTCCGAAGAA GACCTACTCG AGATGGGCGT GATTACGGAT TCACTGGCCG TCGTTTTACA  1500
AAGGCTTCTT CTGGATGAGC TCTACCCGCA CTAATGCCTA AGTGACCGGC AGCAAAATGT  1500

ACGTCGTGAC TGGGAAAACC CTGGCGTTAC CCAACTTAAT CGCCTTGCAG CACATCCCCC  1560
TGCAGCACTG ACCCTTTTGG GACCGCAATG GGTTGAATTA GCGGAACGTC GTGTAGGGGG  1560
```

FIG.13B-2

pICAST OMN

```
TTTCGCCAGC TGGCGTAATA GCGAAGAGGC CCGCACCGAT CGCCCTTCCC AACAGTTACG   1620
AAAGCGGTCG ACCGCATTAT CGCTTCTCCG GGCGTGGCTA GCGGGAAGGG TTGTCAATGC   1620

CAGCCTGAAT GGCGAATGGC GCTTTGCCTG GTTTCCGGCA CCAGAAGCGG TGCCGGAAAG   1680
GTCGGACTTA CCGCTTACCG CGAAACGGAC CAAAGGCCGT GGTCTTCGCC ACGGCCTTTC   1680

CTGGCTGGAG TGCGATCTTC CTGAGGCCGA TACTGTCGTC GTCCCCTCAA ACTGGCAGAT   1740
GACCGACCTC ACGCTAGAAG GACTCCGGCT ATGACAGCAG CAGGGGAGTT TGACCGTCTA   1740

GCACGGTTAC GATGCGCCCA TCTACACCAA CGTGACCTAT CCCATTACGG TCAATCCGCC   1800
CGTGCCAATG CTACGCGGGT AGATGTGGTT GCACTGGATA GGGTAATGCC AGTTAGGCGG   1800

GTTTGTTCCC ACGGAGAATC CGACGGGTTG TTACTCGCTC ACATTTAATG TTGATGAAAG   1860
CAAACAAGGG TGCCTCTTAG GCTGCCCAAC AATGAGCGAG TGTAAATTAC AACTACTTTC   1860

CTGGCTACAG GAAGGCCAGA CGCGAATTAT TTTTGATGGC GTTAACTCGG CGTTTCATCT   1920
GACCGATGTC CTTCCGGTCT GCGCTTAATA AAAACTACCG CAATTGAGCC GCAAAGTAGA   1920

GTGGTGCAAC GGGCGCTGGG TCGGTTACGG CCAGGACAGT CGTTTGCCGT CTGAATTTGA   1980
CACCACGTTG CCCGCGACCC AGCCAATGCC GGTCCTGTCA GCAAACGGCA GACTTAAACT   1980

CCTGAGCGCA TTTTTACGCG CCGGAGAAAA CCGCCTCGCG GTGATGGTGC TGCGCTGGAG   2040
GGACTCGCGT AAAAATGCGC GGCCTCTTTT GGCGGAGCGC CACTACCACG ACGCGACCTC   2040

TGACGGCAGT TATCTGGAAG ATCAGGATAT GTGGCGGATG AGCGGCATTT TCCGTGACGT   2100
ACTGCCGTCA ATAGACCTTC TAGTCCTATA CACCGCCTAC TCGCCGTAAA AGGCACTGCA   2100

CTCGTTGCTG CATAAACCGA CTACACAAAT CAGCGATTTC CATGTTGCCA CTCGCTTTAA   2160
GAGCAACGAC GTATTTGGCT GATGTGTTTA GTCGCTAAAG GTACAACGGT GAGCGAAATT   2160

TGATGATTTC AGCCGCGCTG TACTGGAGGC TGAAGTTCAG ATGTGCGGCG AGTTGCGTGA   2220
ACTACTAAAG TCGGCGCGAC ATGACCTCCG ACTTCAAGTC TACACGCCGC TCAACGCACT   2220

CTACCTACGG GTAACAGTTT CTTTATGGCA GGGTGAAACG CAGGTCGCCA GCGGCACCGC   2280
GATGGATGCC CATTGTCAAA GAAATACCGT CCCACTTTGC GTCCAGCGGT CGCCGTGGCG   2280

GCCTTTCGGC GGTGAAATTA TCGATGAGCG TGGTGGTTAT GCCGATCGCG TCACACTACG   2340
CGGAAAGCCG CCACTTTAAT AGCTACTCGC ACCACCAATA CGGCTAGCGC AGTGTGATGC   2340
```

FIG.13B-3

```
TCTGAACGTC GAAAACCCGA AACTGTGGAG CGCCGAAATC CCGAATCTCT ATCGTGCGGT   2400
AGACTTGCAG CTTTTGGGCT TTGACACCTC GCGGCTTTAG GGCTTAGAGA TAGCACGCCA   2400

GGTTGAACTG CACACCGCCG ACGGCACGCT GATTGAAGCA GAAGCCTGCG ATGTCGGTTT   2460
CCAACTTGAC GTGTGGCGGC TGCCGTGCGA CTAACTTCGT CTTCGGACGC TACAGCCAAA   2460

CCGCGAGGTG CGGATTGAAA ATGGTCTGCT GCTGCTGAAC GGCAAGCCGT TGCTGATTCG   2520
GGCGCTCCAC GCCTAACTTT TACCAGACGA CGACGACTTG CCGTTCGGCA ACGACTAAGC   2520

AGGCGTTAAC CGTCACGAGC ATCATCCTCT GCATGGTCAG GTCATGGATG AGCAGACGAT   2580
TCCGCAATTG GCAGTGCTCG TAGTAGGAGA CGTACCAGTC CAGTACCTAC TCGTCTGCTA   2580

GGTGCAGGAT ATCCTGCTGA TGAAGCAGAA CAACTTTAAC GCCGTGCGCT GTTCGCATTA   2640
CCACGTCCTA TAGGACGACT ACTTCGTCTT GTTGAAATTG CGGCACGCGA CAAGCGTAAT   2640

TCCGAACCAT CCGCTGTGGT ACACGCTGTG CGACCGCTAC GGCCTGTATG TGGTGGATGA   2700
AGGCTTGGTA GGCGACACCA TGTGCGACAC GCTGGCGATG CCGGACATAC ACCACCTACT   2700

AGCCAATATT GAAACCCACG GCATGGTGCC AATGAATCGT CTGACCGATG ATCCGCGCTG   2760
TCGGTTATAA CTTTGGGTGC CGTACCACGG TTACTTAGCA GACTGGCTAC TAGGCGCGAC   2760

GCTACCGGCG ATGAGCGAAC GCGTAACGCG AATGGTGCAG CGCGATCGTA ATCACCCGAG   2820
CGATGGCCGC TACTCGCTTG CGCATTGCGC TTACCACGTC GCGCTAGCAT TAGTGGGCTC   2820

TGTGATCATC TGGTCGCTGG GGAATGAATC AGGCCACGGC GCTAATCACG ACGCGCTGTA   2880
ACACTAGTAG ACCAGCGACC CCTTACTTAG TCCGGTGCCG CGATTAGTGC TGCGCGACAT   2880

TCGCTGGATC AAATCTGTCG ATCCTTCCCG CCCGGTGCAG TATGAAGGCG GCGGAGCCGA   2940
AGCGACCTAG TTTAGACAGC TAGGAAGGGC GGGCCACGTC ATACTTCCGC CGCCTCGGCT   2940

CACCACGGCC ACCGATATTA TTTGCCCGAT GTACGCGCGC GTGGATGAAG ACCAGCCCTT   3000
GTGGTGCCGG TGGCTATAAT AAACGGGCTA CATGCGCGCG CACCTACTTC TGGTCGGGAA   3000

CCCGGCTGTG CCGAAATGGT CCATCAAAAA ATGGCTTTCG CTACCTGGAG AGACGCGCCC   3060
GGGCCGACAC GGCTTTACCA GGTAGTTTTT TACCGAAAGC GATGGACCTC TCTGCGCGGG   3060

GCTGATCCTT TGCGAATACG CCCACGCGAT GGGTAACAGT CTTGGCGGTT TCGCTAAATA   3120
CGACTAGGAA ACGCTTATGC GGGTGCGCTA CCCATTGTCA GAACCGCCAA AGCGATTTAT   3120
```

FIG.13B-4

```
CTGGCAGGCG TTTCGTCAGT ATCCCCGTTT ACAGGGCGGC TTCGTCTGGG ACTGGGTGGA   3180
GACCGTCCGC AAAGCAGTCA TAGGGGCAAA TGTCCCGCCG AAGCAGACCC TGACCCACCT   3180

TCAGTCGCTG ATTAAATATG ATGAAAACGG CAACCCGTGG TCGGCTTACG GCGGTGATTT   3240
AGTCAGCGAC TAATTTATAC TACTTTTGCC GTTGGGCACC AGCCGAATGC CGCCACTAAA   3240

TGGCGATACG CCGAACGATC GCCAGTTCTG TATGAACGGT CTGGTCTTTG CCGACCGCAC   3300
ACCGCTATGC GGCTTGCTAG CGGTCAAGAC ATACTTGCCA GACCAGAAAC GGCTGGCGTG   3300

GCCGCATCCA GCGCTGACGG AAGCAAAACA CCAGCAGCAG TTTTTCCAGT TCCGTTTATC   3360
CGGCGTAGGT CGCGACTGCC TTCGTTTTGT GGTCGTCGTC AAAAAGGTCA AGGCAAATAG   3360

CGGGCAAACC ATCGAAGTGA CCAGCGAATA CCTGTTCCGT CATAGCGATA ACGAGCTCCT   3420
GCCCGTTTGG TAGCTTCACT GGTCGCTTAT GGACAAGGCA GTATCGCTAT TGCTCGAGGA   3420

GCACTGGATG GTGGCGCTGG ATGGTAAGCC GCTGGCAAGC GGTGAAGTGC CTCTGGATGT   3480
CGTGACCTAC CACCGCGACC TACCATTCGG CGACCGTTCG CCACTTCACG GAGACCTACA   3480

CGCTCCACAA GGTAAACAGT TGATTGAACT GCCTGAACTA CCGCAGCCGG AGAGCGCCGG   3540
GCGAGGTGTT CCATTTGTCA ACTAACTTGA CGGACTTGAT GGCGTCGGCC TCTCGCGGCC   3540

GCAACTCTGG CTCACAGTAC GCGTAGTGCA ACCGAACGCG ACCGCATGGT CAGAAGCCGG   3600
CGTTGAGACC GAGTGTCATG CGCATCACGT TGGCTTGCGC TGGCGTACCA GTCTTCGGCC   3600

GCACATCAGC GCCTGGCAGC AGTGGCGTCT GGCGGAAAAC CTCAGTGTGA CGCTCCCCGC   3660
CGTGTAGTCG CGGACCGTCG TCACCGCAGA CCGCCTTTTG GAGTCACACT GCGAGGGGCG   3660

CGCGTCCCAC GCCATCCCGC ATCTGACCAC CAGCGAAATG GATTTTTGCA TCGAGCTGGG   3720
GCGCAGGGTG CGGTAGGGCG TAGACTGGTG GTCGCTTTAC CTAAAAACGT AGCTCGACCC   3720

TAATAAGCGT TGGCAATTTA ACCGCCAGTC AGGCTTTCTT TCACAGATGT GGATTGGCGA   3780
ATTATTCGCA ACCGTTAAAT TGGCGGTCAG TCCGAAAGAA AGTGTCTACA CCTAACCGCT   3780

TAAAAAACAA CTGCTGACGC CGCTGCGCGA TCAGTTCACC CGTGTCGATA GATCTGGAGG   3840
ATTTTTTGTT GACGACTGCG GCGACGCGCT AGTCAAGTGG GCACAGCTAT CTAGACCTCC   3840

TGGTGGCAGC AGGCCTTGGC GCGCCGGATC CTTAATTAAC AATTGACCGG TAATAATAGG   3900
ACCACCGTCG TCCGGAACCG CGCGGCCTAG GAATTAATTG TTAACTGGCC ATTATTATCC   3900
```

FIG. 13B-5

```
TAGATAAGTG ACTGATTAGA TGCATTTCGA CTAGATCCCT CGACCAATTC CGGTTATTTT   3960
ATCTATTCAC TGACTAATCT ACGTAAAGCT GATCTAGGGA GCTGGTTAAG GCCAATAAAA   3960

CCACCATATT GCCGTCTTTT GGCAATGTGA GGGCCCGGAA ACCTGGCCCT GTCTTCTTGA   4020
GGTGGTATAA CGGCAGAAAA CCGTTACACT CCCGGGCCTT TGGACCGGGA CAGAAGAACT   4020

CGAGCATTCC TAGGGGTCTT TCCCCTCTCG CCAAAGGAAT GCAAGGTCTG TTGAATGTCG   4080
GCTCGTAAGG ATCCCCAGAA AGGGGAGAGC GGTTTCCTTA CGTTCCAGAC AACTTACAGC   4080

TGAAGGAAGC AGTTCCTCTG GAAGCTTCTT GAAGACAAAC AACGTCTGTA GCGACCCTTT   4140
ACTTCCTTCG TCAAGGAGAC CTTCGAAGAA CTTCTGTTTG TTGCAGACAT CGCTGGGAAA   4140

GCAGGCAGCG GAACCCCCCA CCTGGCGACA GGTGCCTCTG CGGCCAAAAG CCACGTGTAT   4200
CGTCCGTCGC CTTGGGGGGT GGACCGCTGT CCACGGAGAC GCCGGTTTTC GGTGCACATA   4200

AAGATACACC TGCAAAGGCG GCACAACCCC AGTGCCACGT TGTGAGTTGG ATAGTTGTGG   4260
TTCTATGTGG ACGTTTCCGC CGTGTTGGGG TCACGGTGCA ACACTCAACC TATCAACACC   4260

AAAGAGTCAA ATGGCTCTCC TCAAGCGTAT TCAACAAGGG GCTGAAGGAT GCCCAGAAGG   4320
TTTCTCAGTT TACCGAGAGG AGTTCGCATA AGTTGTTCCC CGACTTCCTA CGGGTCTTCC   4320

TACCCCATTG TATGGGATCT GATCTGGGGC CTCGGTGCAC ATGCTTTACA TGTGTTTAGT   4380
ATGGGGTAAC ATACCCTAGA CTAGACCCCG GAGCCACGTG TACGAAATGT ACACAAATCA   4380

CGAGGTTAAA AAACGTCTAG GCCCCCCGAA CCACGGGGAC GTGGTTTTCC TTTGAAAAAC   4440
GCTCCAATTT TTTGCAGATC CGGGGGGCTT GGTGCCCCTG CACCAAAAGG AAACTTTTTG   4440

ACGATGATAA TACCATGAAA AAGCCTGAAC TCACCGCGAC GTCTGTCGAG AAGTTTCTGA   4500
TGCTACTATT ATGGTACTTT TTCGGACTTG AGTGGCGCTG CAGACAGCTC TTCAAAGACT   4500

TCGAAAAGTT CGACAGCGTC TCCGACCTGA TGCAGCTCTC GGAGGGCGAA GAATCTCGTG   4560
AGCTTTTCAA GCTGTCGCAG AGGCTGGACT ACGTCGAGAG CCTCCCGCTT CTTAGAGCAC   4560

CTTTCAGCTT CGATGTAGGA GGGCGTGGAT ATGTCCTGCG GGTAAATAGC TGCGCCGATG   4620
GAAAGTCGAA GCTACATCCT CCCGCACCTA TACAGGACGC CCATTTATCG ACGCGGCTAC   4620

GTTTCTACAA AGATCGTTAT GTTTATCGGC ACTTTGCATC GGCCGCGCTC CCGATTCCGG   4680
CAAAGATGTT TCTAGCAATA CAAATAGCCG TGAAACGTAG CCGGCGCGAG GGCTAAGGCC   4680
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FIG. 13B-6

```
AAGTGCTTGA CATTGGGGAA TTTAGCGAGA GCCTGACCTA TTGCATCTCC CGCCGTGCAC   4740
TTCACGAACT GTAACCCCTT AAATCGCTCT CGGACTGGAT AACGTAGAGG GCGGCACGTG   4740

AGGGTGTCAC GTTGCAAGAC CTGCCTGAAA CCGAACTGCC CGCTGTTCTG CAGCCGGTCG   4800
TCCCACAGTG CAACGTTCTG GACGGACTTT GGCTTGACGG GCGACAAGAC GTCGGCCAGC   4800

CGGAGGCCAT GGATGCGATC GCTGCGGCCG ATCTTAGCCA GACGAGCGGG TTCGGCCCAT   4860
GCCTCCGGTA CCTACGCTAG CGACGCCGGC TAGAATCGGT CTGCTCGCCC AAGCCGGGTA   4860

TCGGACCGCA AGGAATCGGT CAATACACTA CATGGCGTGA TTTCATATGC GCGATTGCTG   4920
AGCCTGGCGT TCCTTAGCCA GTTATGTGAT GTACCGCACT AAAGTATACG CGCTAACGAC   4920

ATCCCCATGT GTATCACTGG CAAACTGTGA TGGACGACAC CGTCAGTGCG TCCGTCGCGC   4980
TAGGGGTACA CATAGTGACC GTTTGACACT ACCTGCTGTG GCAGTCACGC AGGCAGCGCG   4980

AGGCTCTCGA TGAGCTGATG CTTTGGGCCG AGGACTGCCC CGAAGTCCGG CACCTCGTGC   5040
TCCGAGAGCT ACTCGACTAC GAAACCCGGC TCCTGACGGG GCTTCAGGCC GTGGAGCACG   5040

ACGCGGATTT CGGCTCCAAC AATGTCCTGA CGGACAATGG CCGCATAACA GCGGTCATTG   5100
TGCGCCTAAA GCCGAGGTTG TTACAGGACT GCCTGTTACC GGCGTATTGT CGCCAGTAAC   5100

ACTGGAGCGA GGCGATGTTC GGGGATTCCC AATACGAGGT CGCCAACATC TTCTTCTGGA   5160
TGACCTCGCT CCGCTACAAG CCCCTAAGGG TTATGCTCCA GCGGTTGTAG AAGAAGACCT   5160

GGCCGTGGTT GGCTTGTATG GAGCAGCAGA CGCGCTACTT CGAGCGGAGG CATCCGGAGC   5220
CCGGCACCAA CCGAACATAC CTCGTCGTCT GCGCGATGAA GCTCGCCTCC GTAGGCCTCG   5220

TTGCAGGATC GCCGCGGCTC CGGGCGTATA TGCTCCGCAT TGGTCTTGAC CAACTCTATC   5280
AACGTCCTAG CGGCGCCGAG GCCCGCATAT ACGAGGCGTA ACCAGAACTG GTTGAGATAG   5280

AGAGCTTGGT TGACGGCAAT TTCGATGATG CAGCTTGGGC GCAGGGTCGA TGCGACGCAA   5340
TCTCGAACCA ACTGCCGTTA AAGCTACTAC GTCGAACCCG CGTCCCAGCT ACGCTGCGTT   5340

TCGTCCGATC CGGAGCCGGG ACTGTCGGGC GTACACAAAT CGCCCGCAGA AGCGCGGCCG   5400
AGCAGGCTAG GCCTCGGCCC TGACAGCCCG CATGTGTTTA GCGGGCGTCT TCGCGCCGGC   5400

TCTGGACCGA TGGCTGTGTA GAAGTACTCG CCGATAGTGG AAACCGACGC CCCAGCACTC   5460
AGACCTGGCT ACCGACACAT CTTCATGAGC GGCTATCACC TTTGGCTGCG GGGTCGTGAG   5460
```

FIG. 13B-7

```
GTCCGAGGGC AAAGGAATAG AGTAGATGCC GACCGGGATC TATCGATAAA ATAAAAGATT   5520
CAGGCTCCCG TTTCCTTATC TCATCTACGG CTGGCCCTAG ATAGCTATTT TATTTTCTAA   5520

TTATTTAGTC TCCAGAAAAA GGGGGGAATG AAGACCCCAA CCTGTAGGTT TGGCAAGCTA   5580
AATAAATCAG AGGTCTTTTT CCCCCCTTAC TTTCTGGGGT GGACATCCAA ACCGTTCGAT   5580

GCTTAAGTAA CGCCATTTTG CAAGGCATGG AAAAATACAT AACTGAGAAT AGAGAAGTTC   5640
CGAATTCATT GCGGTAAAAC GTTCCGTACC TTTTTATGTA TTGACTCTTA TCTCTTCAAG   5640

AGATCAAGGT CAGGAACAGA TGGAACAGCT GAATATGGGC CAAACAGGAT ATCTGTGGTA   5700
TCTAGTTCCA GTCCTTGTCT ACCTTGTCGA CTTATACCCG GTTTGTCCTA TAGACACCAT   5700

AGCAGTTCCT GCCCCGGCTC AGGGCCAAGA ACAGATGGAA CAGCTGAATA TGGGCCAAAC   5760
TCGTCAAGGA CGGGGCCGAG TCCCGGTTCT TGTCTACCTT GTCGACTTAT ACCCGGTTTG   5760

AGGATATCTG TGGTAAGCAG TTCCTGCCCC GGCTCAGGGC CAAGAACAGA TGGTCCCCAG   5820
TCCTATAGAC ACCATTCGTC AAGGACGGGG CCGAGTCCCG GTTCTTGTCT ACCAGGGGTC   5820

ATGCGGTCCA GCCCTCAGCA GTTTCTAGAG AACCATCAGA TGTTTCCAGG GTGCCCCAAG   5880
TACGCCAGGT CGGGAGTCGT CAAAGATCTC TTGGTAGTCT ACAAAGGTCC CACGGGGTTC   5880

GACCTGAAAT GACCCTGTGC CTTATTTGAA CTAACCAATC AGTTCGCTTC TCGCTTCTGT   5940
CTGGACTTTA CTGGGACACG GAATAAACTT GATTGGTTAG TCAAGCGAAG AGCGAAGACA   5940

TCGCGCGCTT CTGCTCCCCG AGCTCAATAA AAGAGCCCAC AACCCCTCAC TCGGGGCGCC   6000
AGCGCGCGAA GACGAGGGGC TCGAGTTATT TTCTCGGGTG TTGGGGAGTG AGCCCCGCGG   6000

AGTCCTCCGA TTGACTGAGT CGCCCGGGTA CCCGTGTATC CAATAAACCC TCTTGCAGTT   6060
TCAGGAGGCT AACTGACTCA GCGGGCCCAT GGGCACATAG GTTATTTGGG AGAACGTCAA   6060

GCATCCGACT TGTGGTCTCG CTGTTCCTTG GGAGGGTCTC CTCTGAGTGA TTGACTACCC   6120
CGTAGGCTGA ACACCAGAGC GACAAGGAAC CCTCCCAGAG GAGACTCACT AACTGATGGG   6120

GTCAGCGGGG GTCTTTCATT CATGCAGCAT GTATCAAAAT TAATTTGGTT TTTTTTCTTA   6180
CAGTCGCCCC CAGAAAGTAA GTACGTCGTA CATAGTTTTA ATTAAACCAA AAAAAAGAAT   6180

AGTATTTACA TTAAATGGCC ATAGTTGCAT TAATGAATCG GCCAACGCGC GGGGAGAGGC   6240
TCATAAATGT AATTTACCGG TATCAACGTA ATTACTTAGC CGGTTGCGCG CCCCTCTCCG   6240
```

FIG.13B-8

```
GGTTTGCGTA TTGGCGCTCT TCCGCTTCCT CGCTCACTGA CTCGCTGCGC TCGGTCGTTC   6300
CCAAACGCAT AACCGCGAGA AGGCGAAGGA GCGAGTGACT GAGCGACGCG AGCCAGCAAG   6300

GGCTGCGGCG AGCGGTATCA GCTCACTCAA AGGCGGTAAT ACGGTTATCC ACAGAATCAG   6360
CCGACGCCGC TCGCCATAGT CGAGTGAGTT TCCGCCATTA TGCCAATAGG TGTCTTAGTC   6360

GGGATAACGC AGGAAAGAAC ATGTGAGCAA AAGGCCAGCA AAAGGCCAGG AACCGTAAAA   6420
CCCTATTGCG TCCTTTCTTG TACACTCGTT TTCCGGTCGT TTTCCGGTCC TTGGCATTTT   6420

AGGCCGCGTT GCTGGCGTTT TTCCATAGGC TCCGCCCCCC TGACGAGCAT CACAAAAATC   6480
TCCGGCGCAA CGACCGCAAA AAGGTATCCG AGGCGGGGGG ACTGCTCGTA GTGTTTTTAG   6480

GACGCTCAAG TCAGAGGTGG CGAAACCCGA CAGGACTATA AAGATACCAG GCGTTTCCCC   6540
CTGCGAGTTC AGTCTCCACC GCTTTGGGCT GTCCTGATAT TTCTATGGTC CGCAAAGGGG   6540

CTGGAAGCTC CCTCGTGCGC TCTCCTGTTC CGACCCTGCC GCTTACCGGA TACCTGTCCG   6600
GACCTTCGAG GGAGCACGCG AGAGGACAAG GCTGGGACGG CGAATGGCCT ATGGACAGGC   6600

CCTTTCTCCC TTCGGGAAGC GTGGCGCTTT CTCATAGCTC ACGCTGTAGG TATCTCAGTT   6660
GGAAAGAGGG AAGCCCTTCG CACCGCGAAA GAGTATCGAG TGCGACATCC ATAGAGTCAA   6660

CGGTGTAGGT CGTTCGCTCC AAGCTGGGCT GTGTGCACGA ACCCCCCGTT CAGCCCGACC   6720
GCCACATCCA GCAAGCGAGG TTCGACCCGA CACACGTGCT TGGGGGGCAA GTCGGGCTGG   6720

GCTGCGCCTT ATCCGGTAAC TATCGTCTTG AGTCCAACCC GGTAAGACAC GACTTATCGC   6780
CGACGCGGAA TAGGCCATTG ATAGCAGAAC TCAGGTTGGG CCATTCTGTG CTGAATAGCG   6780

CACTGGCAGC AGCCACTGGT AACAGGATTA GCAGAGCGAG GTATGTAGGC GGTGCTACAG   6840
GTGACCGTCG TCGGTGACCA TTGTCCTAAT CGTCTCGCTC CATACATCCG CCACGATGTC   6840

AGTTCTTGAA GTGGTGGCCT AACTACGGCT ACACTAGAAG AACAGTATTT GGTATCTGCG   6900
TCAAGAACTT CACCACCGGA TTGATGCCGA TGTGATCTTC TTGTCATAAA CCATAGACGC   6900

CTCTGCTGAA GCCAGTTACC TTCGGAAAAA GAGTTGGTAG CTCTTGATCC GGCAAACAAA   6960
GAGACGACTT CGGTCAATGG AAGCCTTTTT CTCAACCATC GAGAACTAGG CCGTTTGTTT   6960

CCACCGCTGG TAGCGGTGGT TTTTTTGTTT GCAAGCAGCA GATTACGCGC AGAAAAAAAG   7020
GGTGGCGACC ATCGCCACCA AAAAAACAAA CGTTCGTCGT CTAATGCGCG TCTTTTTTTC   7020
```

FIG.13B-9

GATCTCAAGA AGATCCTTTG ATCTTTTCTA CGGGGTCTGA CGCTCAGTGG AACGAAAACT 7080
CTAGAGTTCT TCTAGGAAAC TAGAAAAGAT GCCCCAGACT GCGAGTCACC TTGCTTTTGA 7080

CACGTTAAGG GATTTTGGTC ATGAGATTAT CAAAAAGGAT CTTCACCTAG ATCCTTTTGC 7140
GTGCAATTCC CTAAAACCAG TACTCTAATA GTTTTTCCTA GAAGTGGATC TAGGAAAACG 7140

GGCCGCAAAT CAATCTAAAG TATATATGAG TAAACTTGGT CTGACAGTTA CCAATGCTTA 7200
CCGGCGTTTA GTTAGATTTC ATATATACTC ATTTGAACCA GACTGTCAAT GGTTACGAAT 7200

ATCAGTGAGG CACCTATCTC AGCGATCTGT CTATTTCGTT CATCCATAGT TGCCTGACTC 7260
TAGTCACTCC GTGGATAGAG TCGCTAGACA GATAAAGCAA GTAGGTATCA ACGGACTGAG 7260

CCCGTCGTGT AGATAACTAC GATACGGGAG GGCTTACCAT CTGGCCCCAG TGCTGCAATG 7320
GGGCAGCACA TCTATTGATG CTATGCCCTC CCGAATGGTA GACCGGGGTC ACGACGTTAC 7320

ATACCGCGAG ACCCACGCTC ACCGGCTCCA GATTTATCAG CAATAAACCA GCCAGCCGGA 7380
TATGGCGCTC TGGGTGCGAG TGGCCGAGGT CTAAATAGTC GTTATTTGGT CGGTCGGCCT 7380

AGGGCCGAGC GCAGAAGTGG TCCTGCAACT TTATCCGCCT CCATCCAGTC TATTAATTGT 7440
TCCCGGCTCG CGTCTTCACC AGGACGTTGA AATAGGCGGA GGTAGGTCAG ATAATTAACA 7440

TGCCGGGAAG CTAGAGTAAG TAGTTCGCCA GTTAATAGTT TGCGCAACGT TGTTGCCATT 7500
ACGGCCCTTC GATCTCATTC ATCAAGCGGT CAATTATCAA ACGCGTTGCA ACAACGGTAA 7500

GCTACAGGCA TCGTGGTGTC ACGCTCGTCG TTTGGTATGG CTTCATTCAG CTCCGGTTCC 7560
CGATGTCCGT AGCACCACAG TGCGAGCAGC AAACCATACC GAAGTAAGTC GAGGCCAAGG 7560

CAACGATCAA GGCGAGTTAC ATGATCCCCC ATGTTGTGCA AAAAAGCGGT TAGCTCCTTC 7620
GTTGCTAGTT CCGCTCAATG TACTAGGGGG TACAACACGT TTTTTCGCCA ATCGAGGAAG 7620

GGTCCTCCGA TCGTTGTCAG AAGTAAGTTG GCCGCAGTGT TATCACTCAT GGTTATGGCA 7680
CCAGGAGGCT AGCAACAGTC TTCATTCAAC CGGCGTCACA ATAGTGAGTA CCAATACCGT 7680

GCACTGCATA ATTCTCTTAC TGTCATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG 7740
CGTGACGTAT TAAGAGAATG ACAGTACGGT AGGCATTCTA CGAAAAGACA CTGACCACTC 7740

TACTCAACCA AGTCATTCTG AGAATAGTGT ATGCGGCGAC CGAGTTGCTC TTGCCCGGCG 7800
ATGAGTTGGT TCAGTAAGAC TCTTATCACA TACGCCGCTG GCTCAACGAG AACGGGCCGC 7800

FIG.13B-10

pICAST OMN

```
TCAATACGGG ATAATACCGC GCCACATAGC AGAACTTTAA AAGTGCTCAT CATTGGAAAA   7860
AGTTATGCCC TATTATGGCG CGGTGTATCG TCTTGAAATT TTCACGAGTA GTAACCTTTT   7860

CGTTCTTCGG GGCGAAAACT CTCAAGGATC TTACCGCTGT TGAGATCCAG TTCGATGTAA   7920
GCAAGAAGCC CCGCTTTTGA GAGTTCCTAG AATGGCGACA ACTCTAGGTC AAGCTACATT   7920

CCCACTCGTG CACCCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT TTCTGGGTGA   7980
GGGTGAGCAC GTGGGTTGAC TAGAAGTCGT AGAAAATGAA AGTGGTCGCA AAGACCCACT   7980

GCAAAAACAG GAAGGCAAAA TGCCGCAAAA AAGGGAATAA GGGCGACACG GAAATGTTGA   8040
CGTTTTTGTC CTTCCGTTTT ACGGCGTTTT TTCCCTTATT CCCGCTGTGC CTTTACAACT   8040

ATACTCATAC TCTTCCTTTT TCAATATTAT TGAAGCATTT ATCAGGGTTA TTGTCTCATG   8100
TATGAGTATG AGAAGGAAAA AGTTATAATA ACTTCGTAAA TAGTCCCAAT AACAGAGTAC   8100

AGCGGATACA TATTTGAATG TATTTAGAAA AATAAACAAA TAGGGGTTCC GCGCACATTT   8160
TCGCCTATGT ATAAACTTAC ATAAATCTTT TTATTTGTTT ATCCCCAAGG CGCGTGTAAA   8160

C                                                                   8161
G                                                                   8161
```

FIG.13B-11

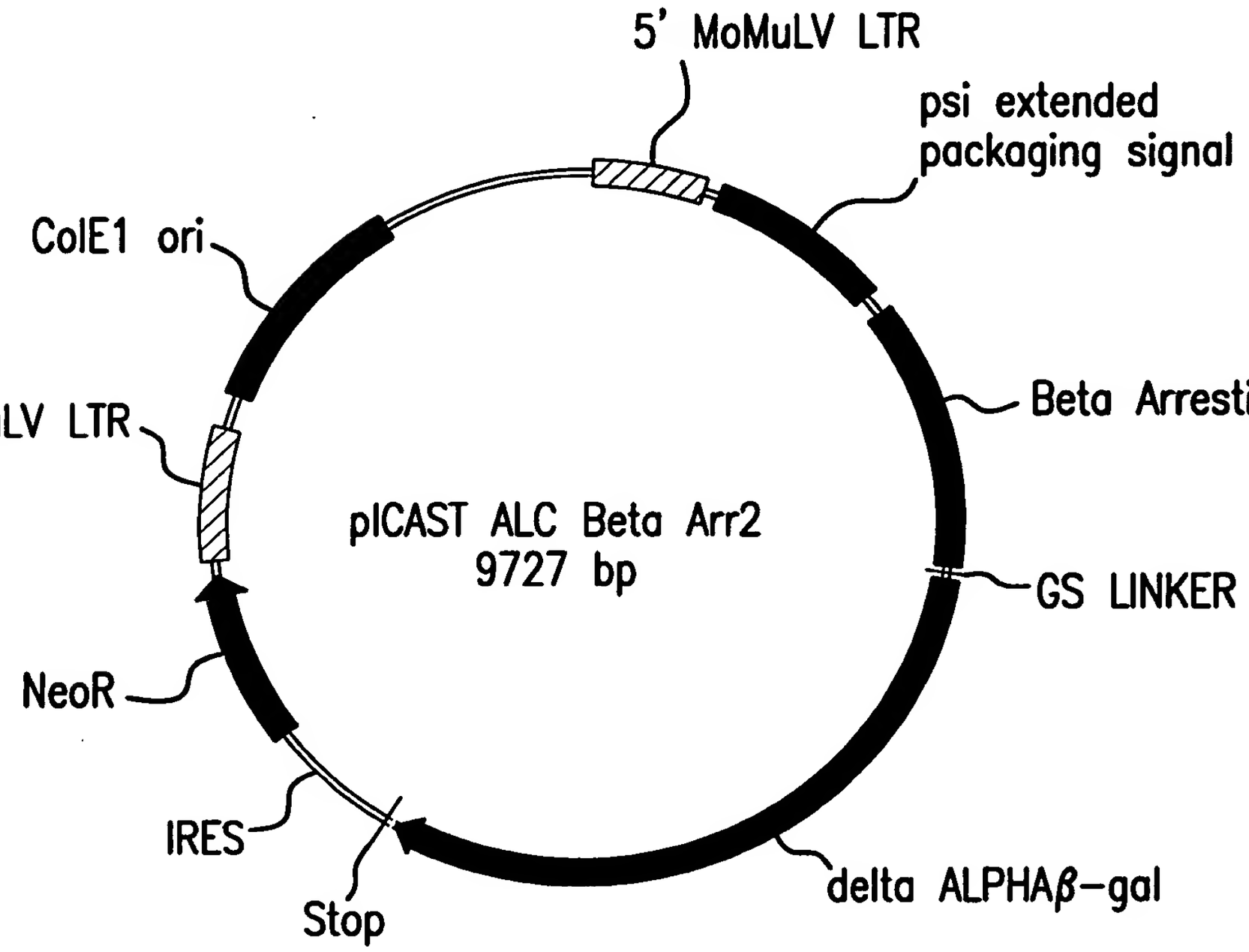

5' MoMuLV LTR
psi extended
packaging signal
ColE1 ori
3' MoMuLV LTR
Beta Arrestin 2
pICAST ALC Beta Arr2
9727 bp
GS LINKER
NeoR
IRES
Stop
delta ALPHAβ-gal

FIG.14

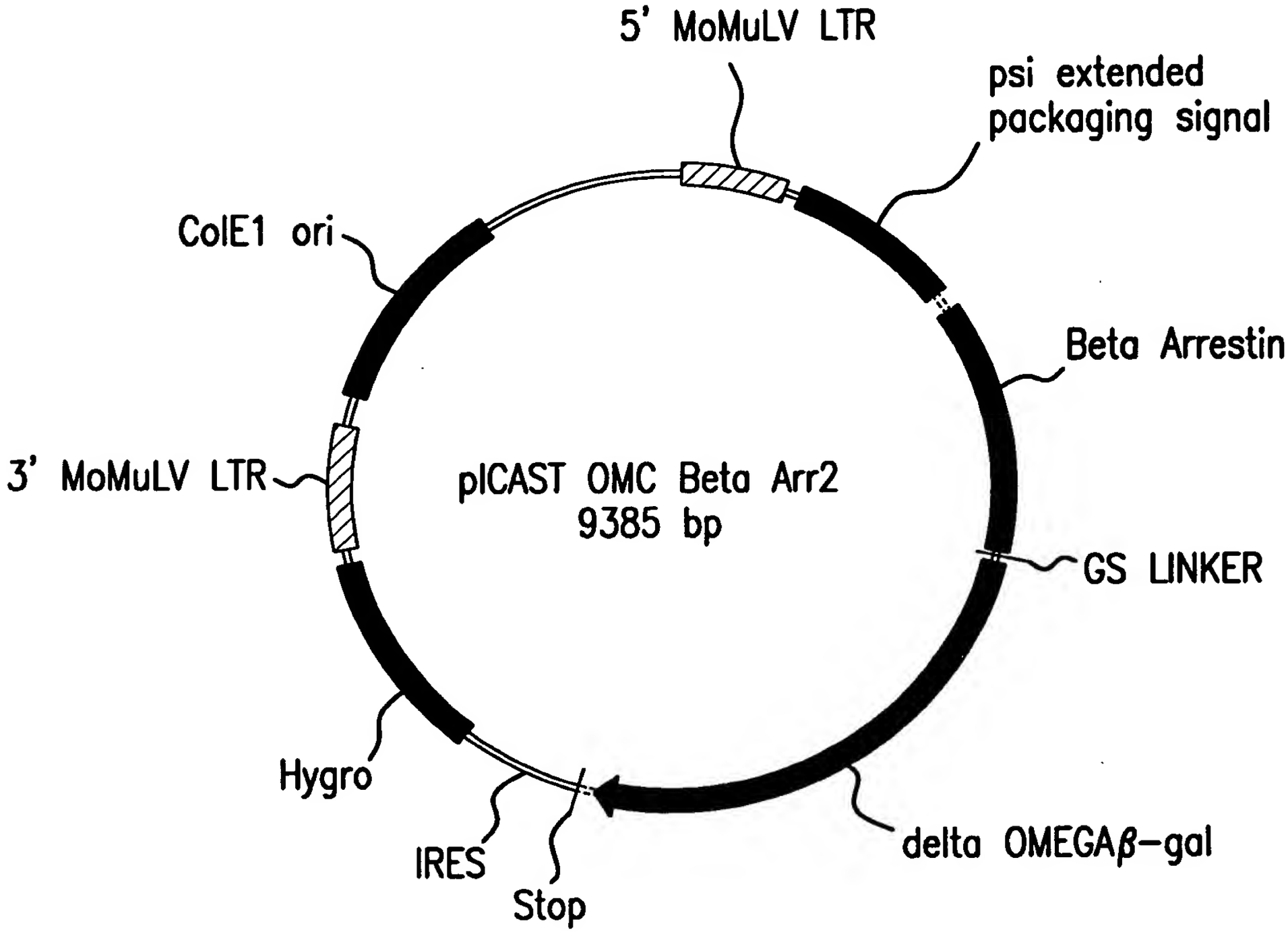


FIG.15

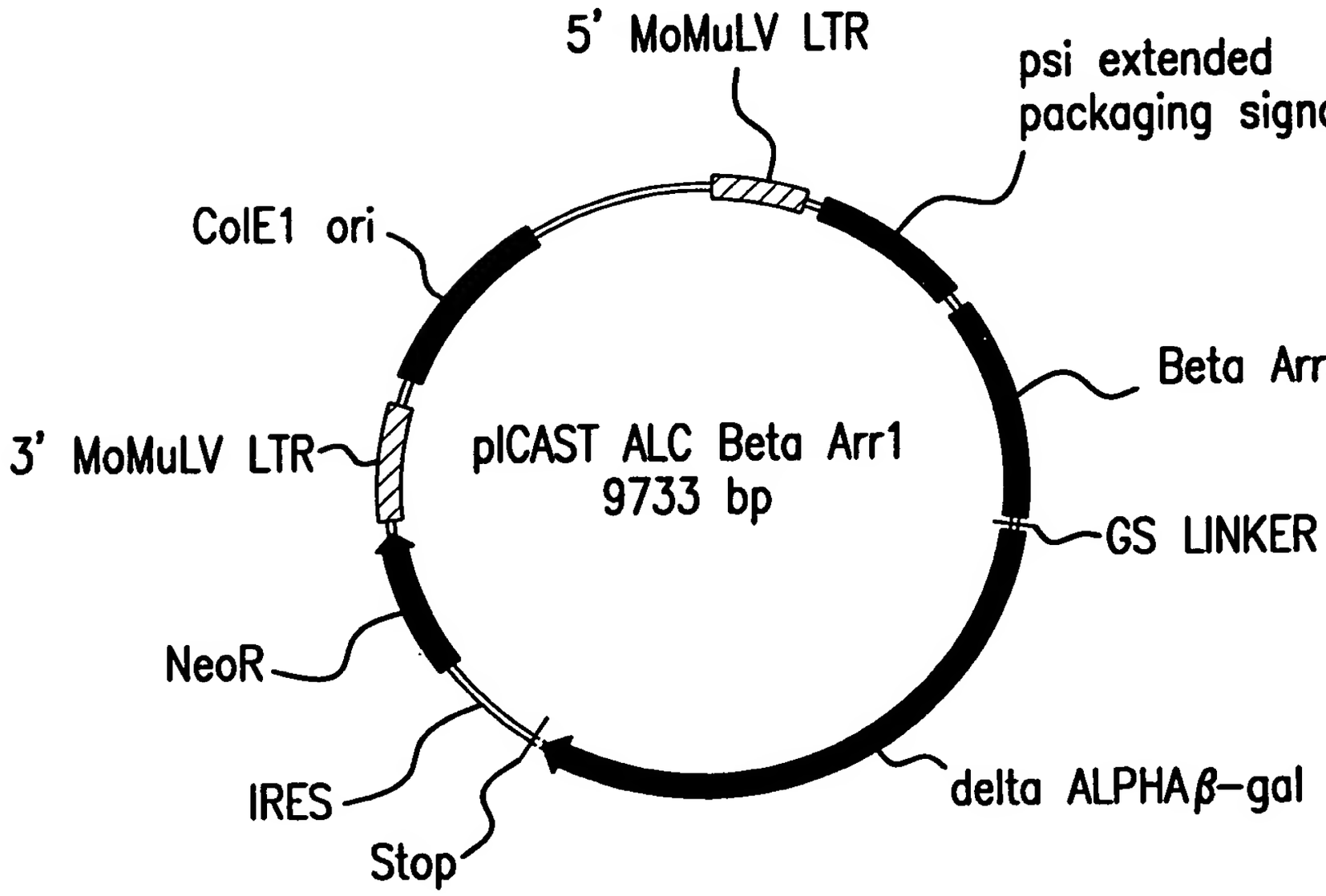


FIG.16

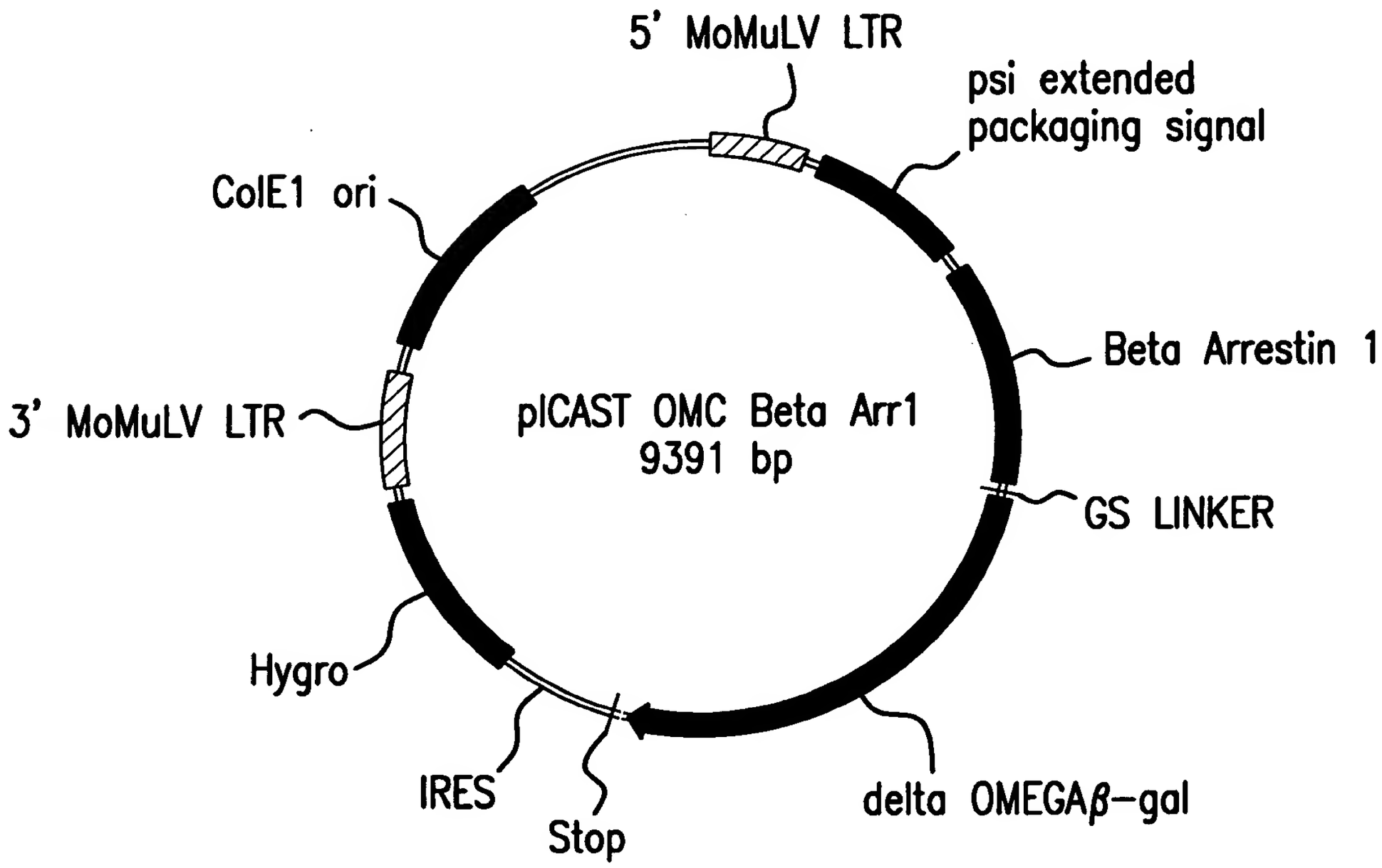

5' MoMuLV LTR
psi extended
packaging signal
ColE1 ori
Beta Arrestin 1
3' MoMuLV LTR
pICAST OMC Beta Arr1
9391 bp
GS LINKER
Hygro
IRES
Stop
delta OMEGAβ-gal

FIG.17

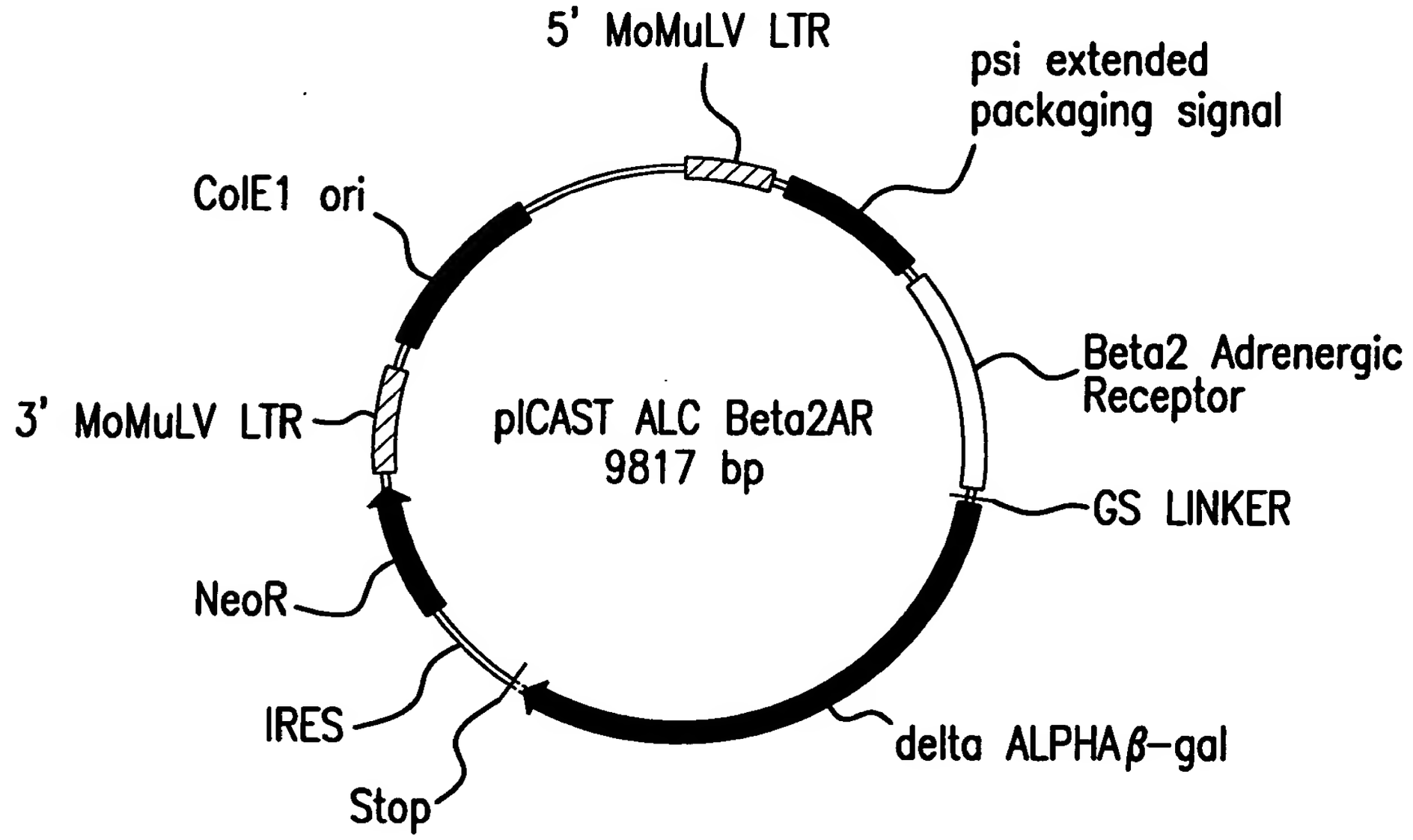


FIG.18

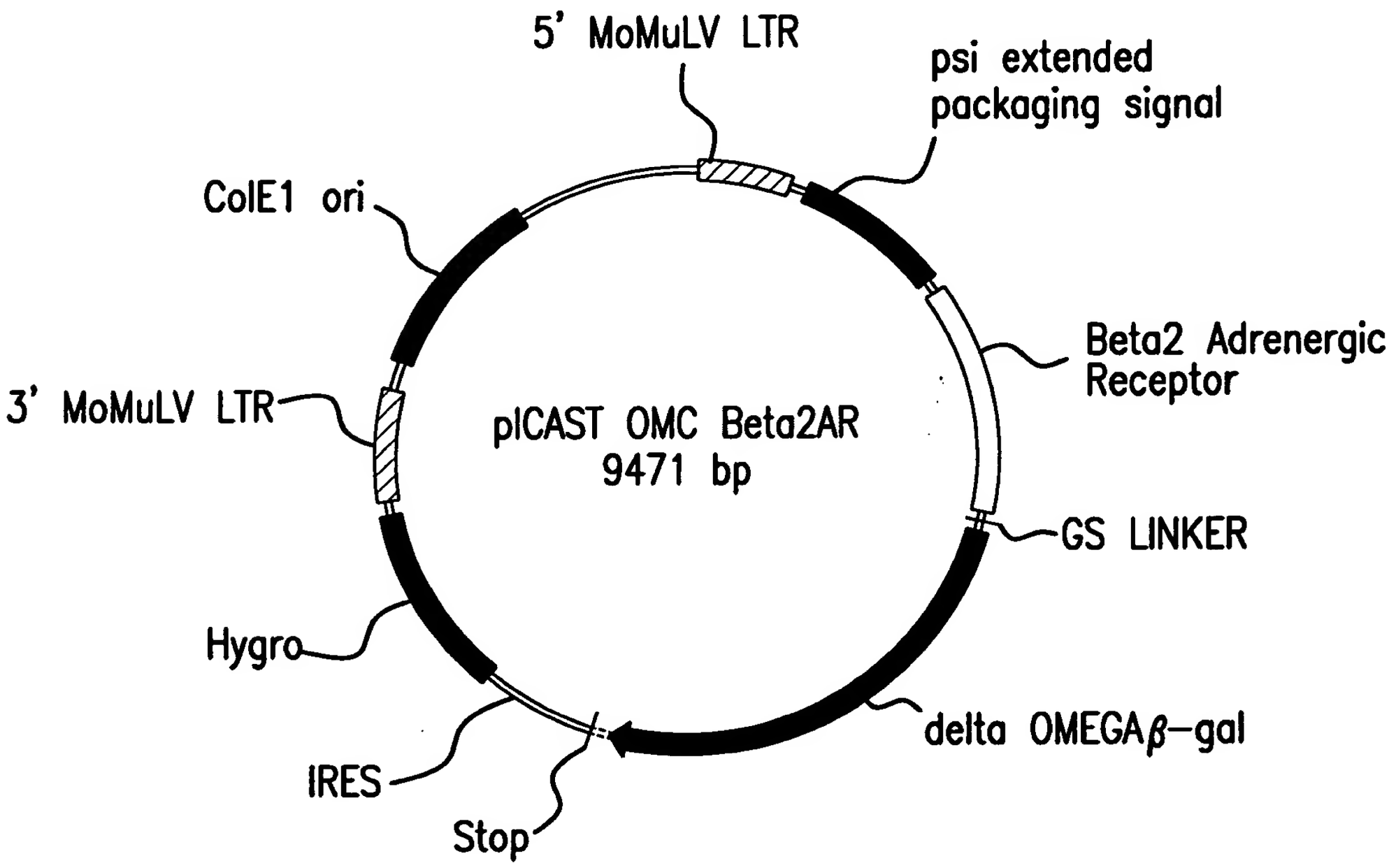

5' MoMuLV LTR
psi extended
packaging signal
ColE1 ori
Beta2 Adrenergic
Receptor
3' MoMuLV LTR
pICAST OMC Beta2AR
9471 bp
GS LINKER
Hygro
delta OMEGAβ–gal
IRES
Stop

FIG.19

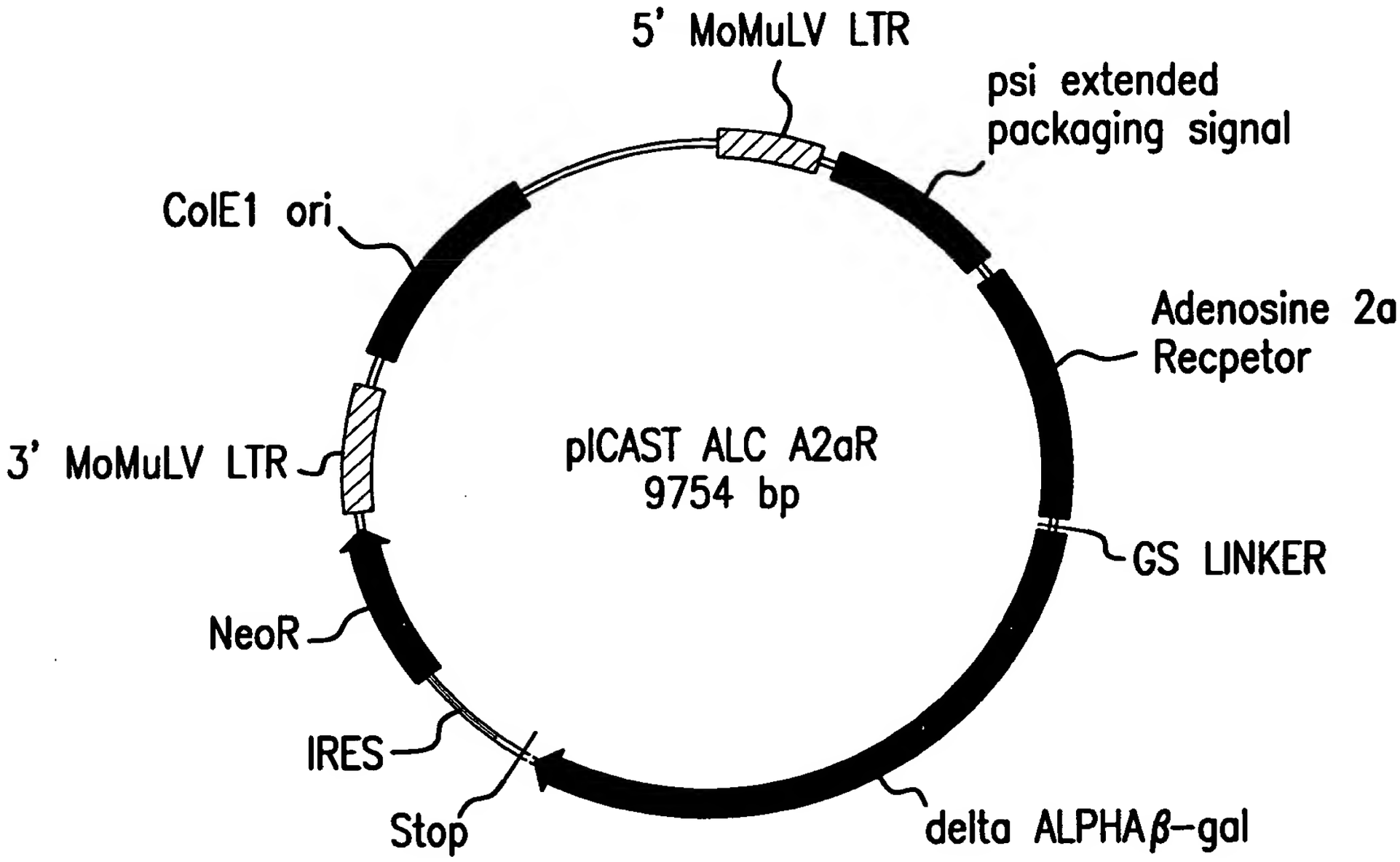

5' MoMuLV LTR
psi extended
packaging signal
ColE1 ori
Adenosine 2a
Recpetor
3' MoMuLV LTR
pICAST ALC A2aR
9754 bp
GS LINKER
NeoR
IRES
Stop
delta ALPHAβ-gal

FIG.20

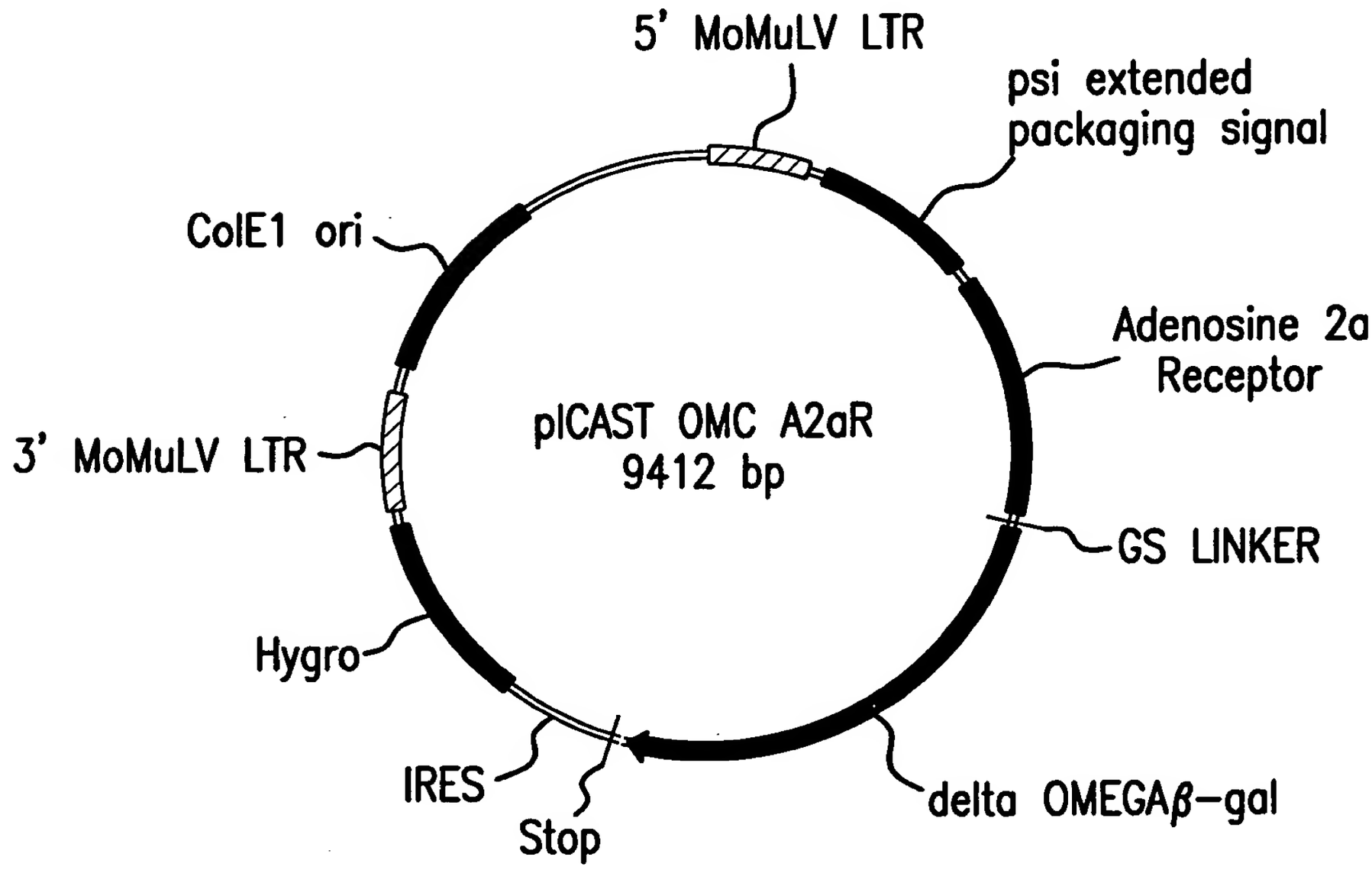


FIG.21

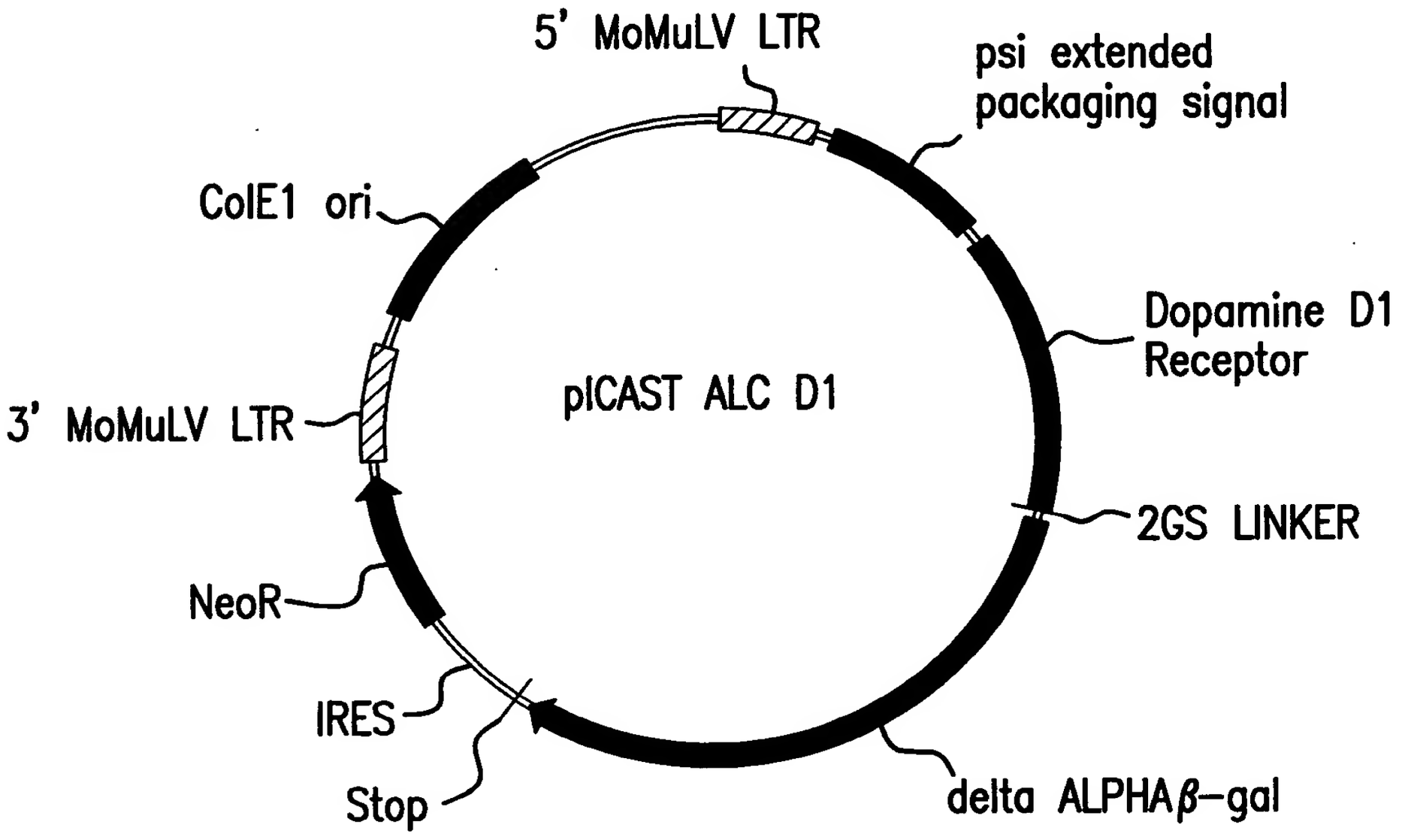


FIG.22

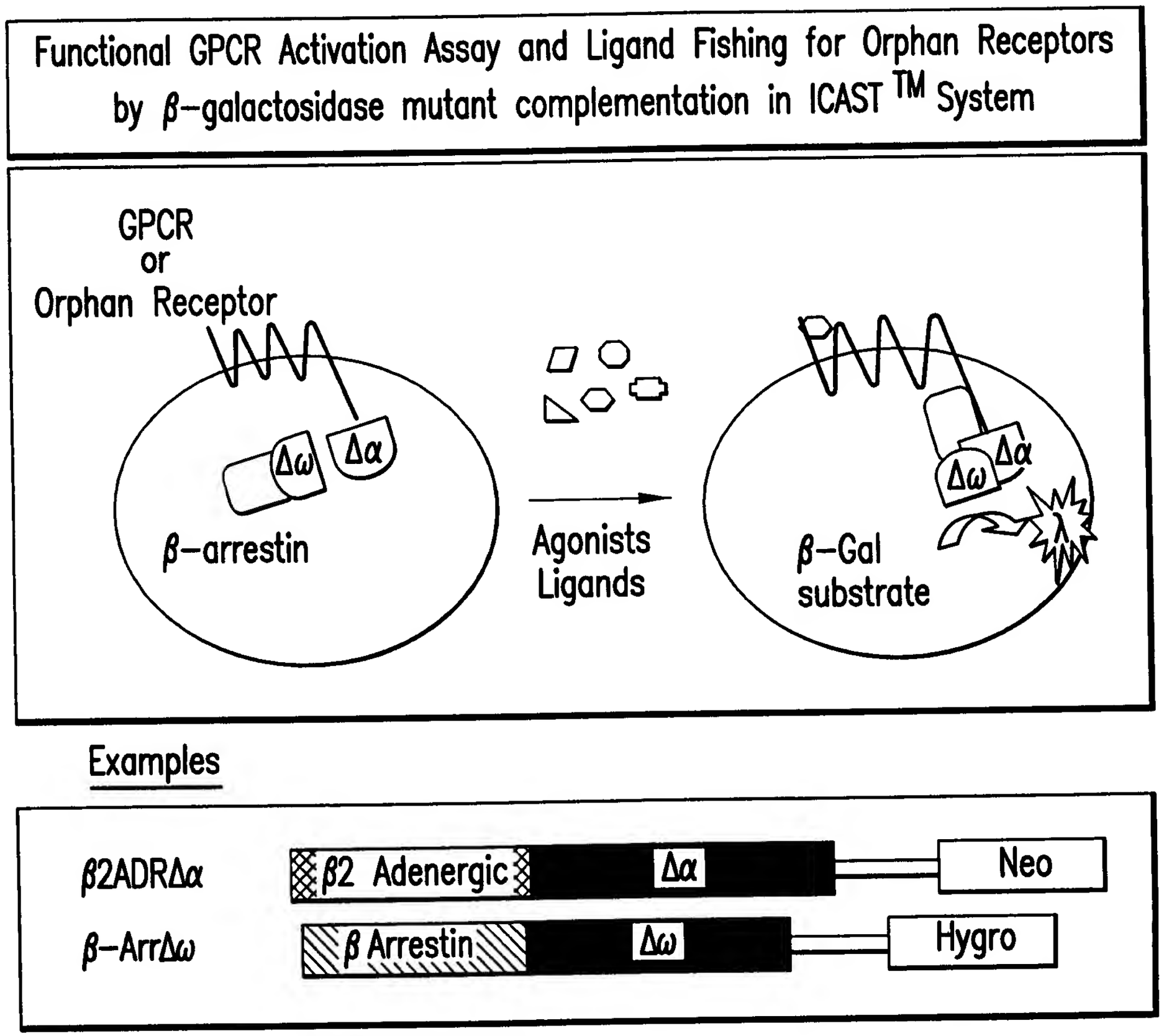
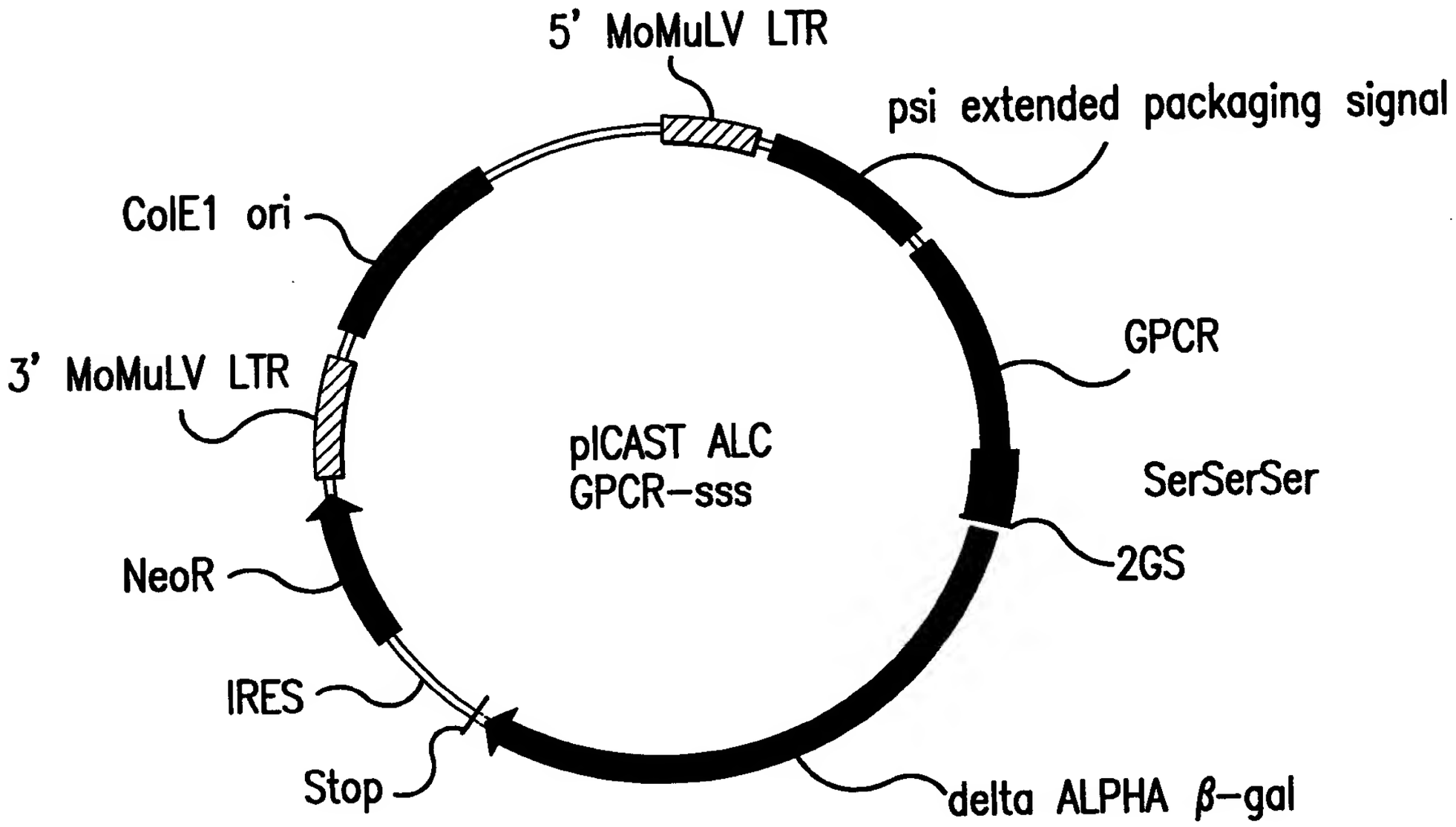
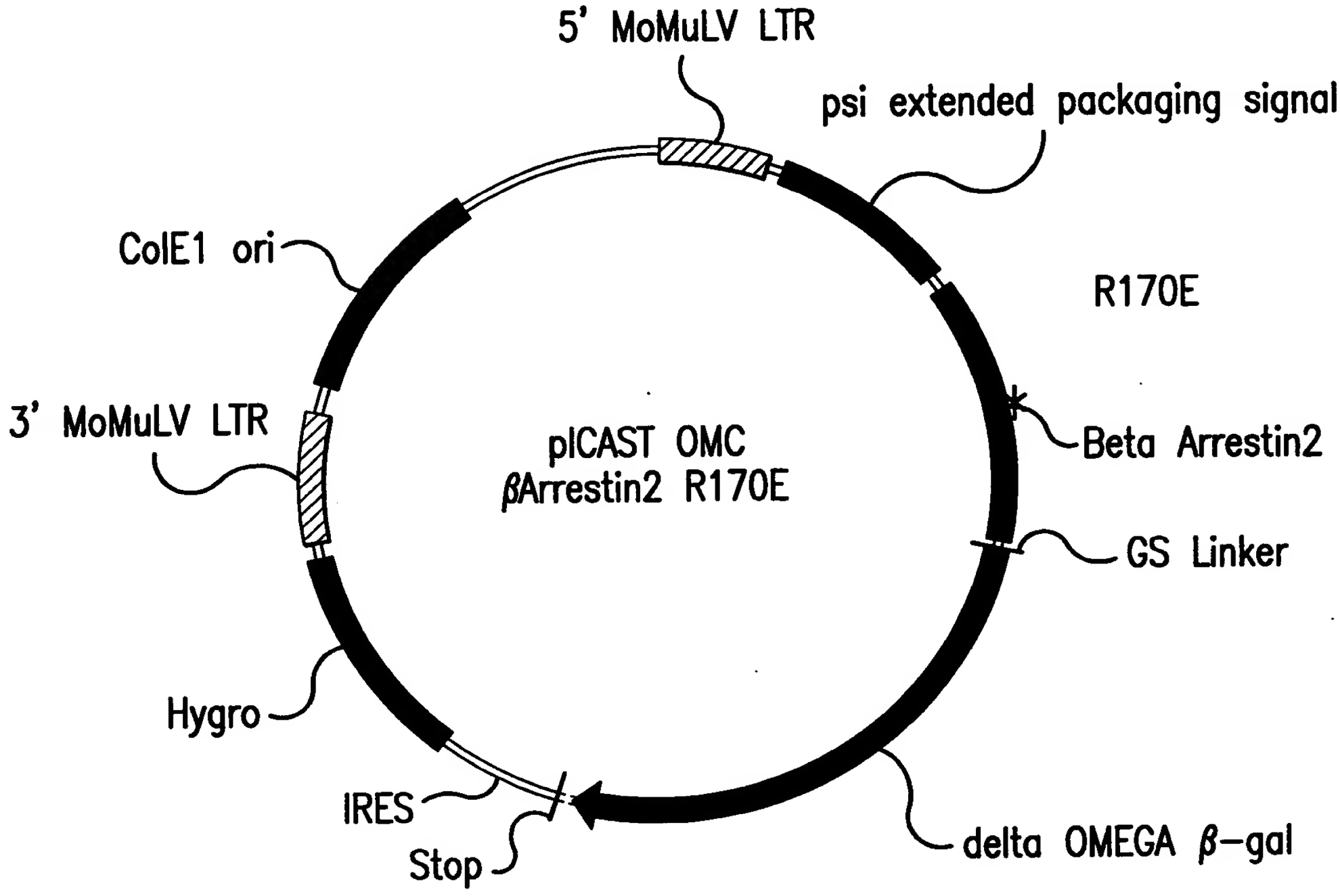

Functional GPCR Activation Assay and Ligand Fishing for Orphan Receptors by β-galactosidase mutant complementation in ICAST TM System
GPCR
or
Orphan Receptor
Δω
Δα
β-arrestin
Agonists
Ligands
Δω
Δα
β-Gal
substrate
Examples
β2ADRΔα
β2 Adenergic
Δα
Neo
β-ArrΔω
β Arrestin
Δω
Hygro

FIG. 23



Vector for Expression of a GPCR with inserted Seronine/Threonine amino acid sequences as a fusion with β-gal Δα.

FIG. 24



Vector for Expression of mutant (R170E) β–arrestin2 as a fusion with β–gal Δω.

FIG. 25

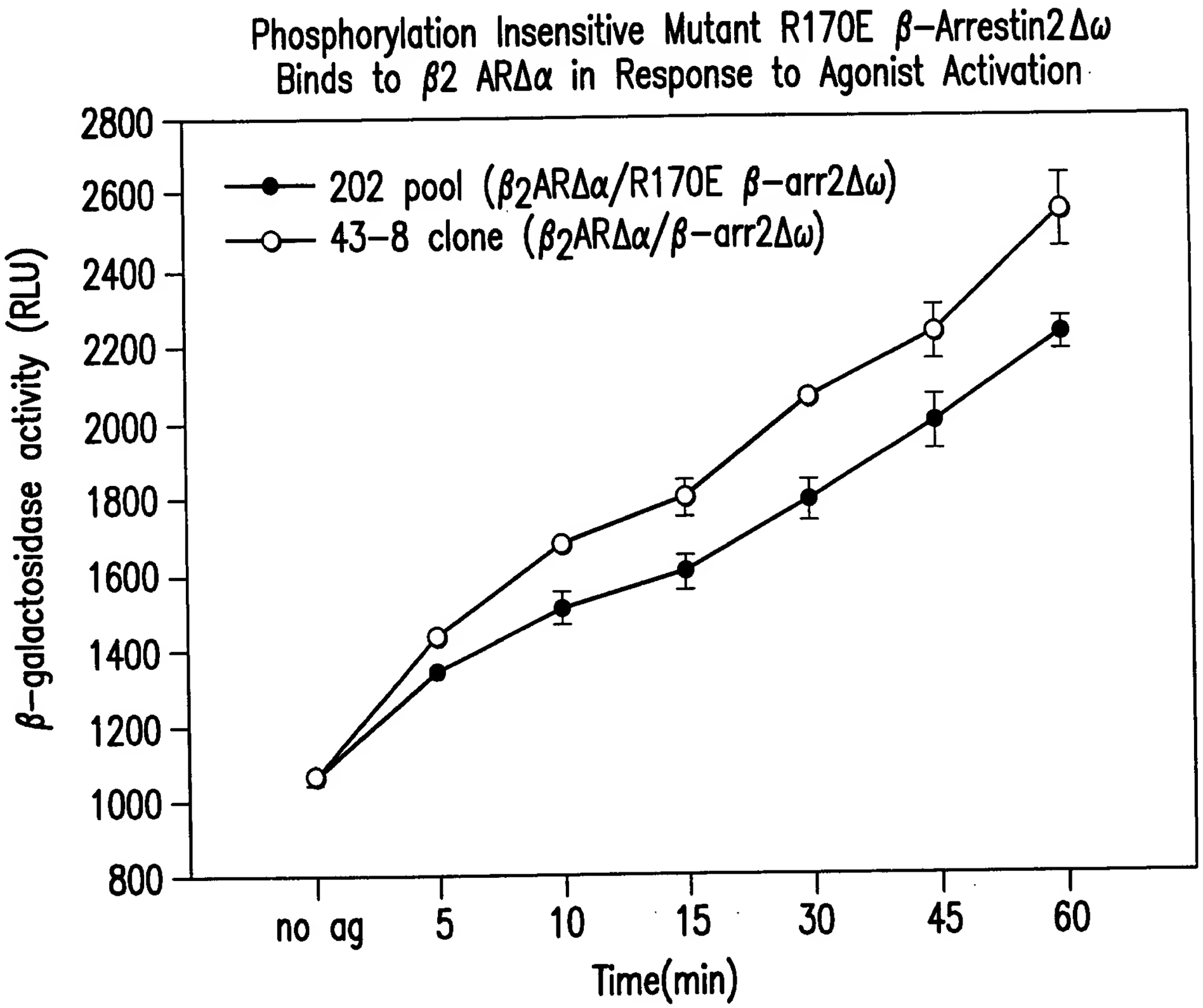
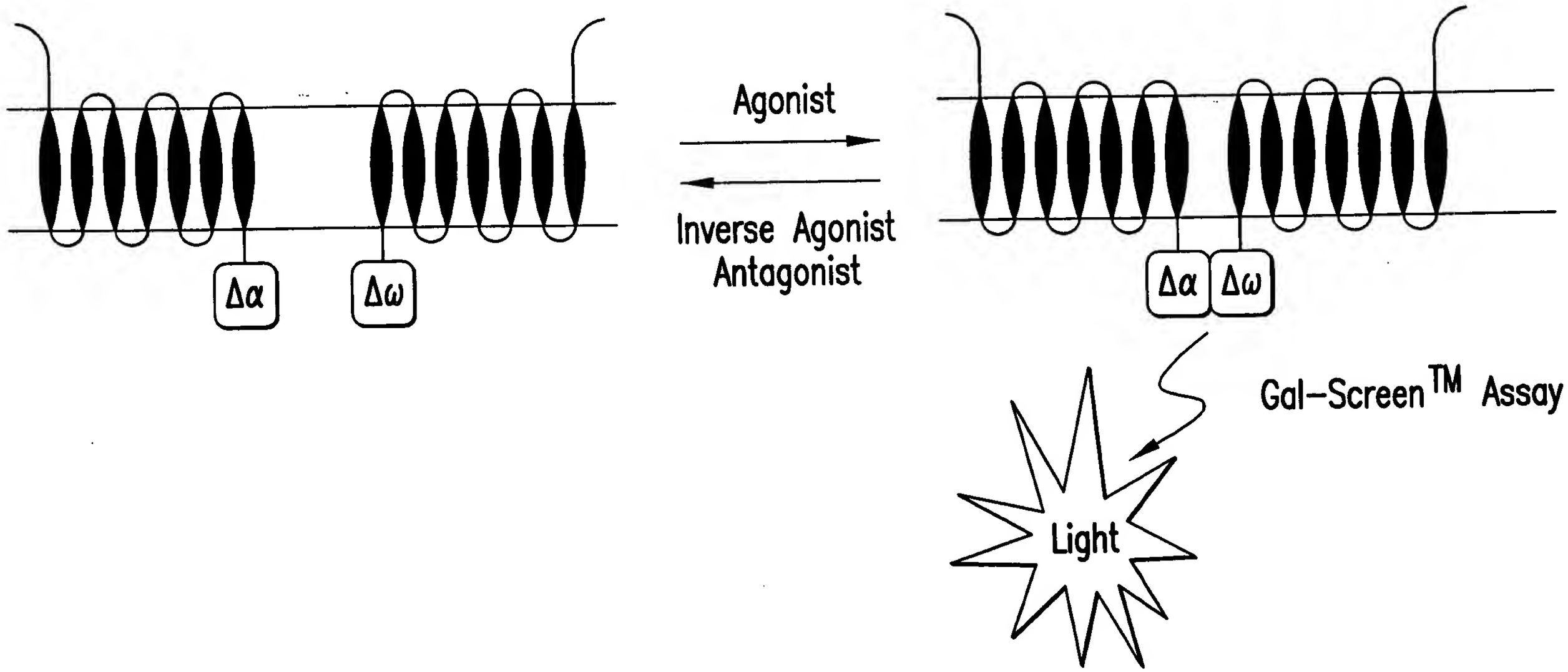

Phosphorylation Insensitive Mutant R170E β–Arrestin2Δω
Binds to β2 ARΔα in Response to Agonist Activation
202 pool (β2ARΔα/R170E β–arr2Δω)
43–8 clone (β2ARΔα/β–arr2Δω)
β–galactosidase activity (RLU)
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
no ag
5
10
15
30
45
60
Time(min)

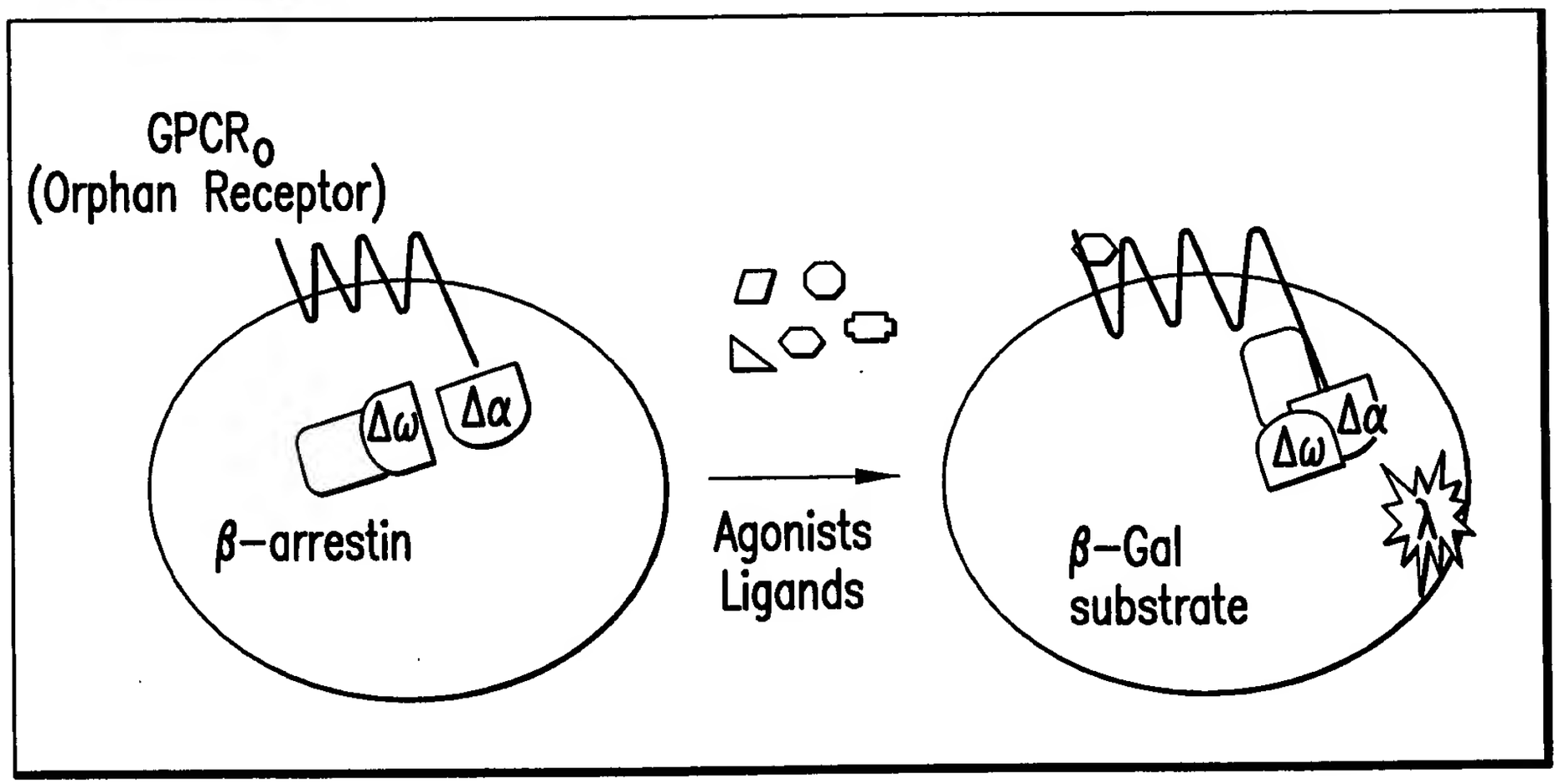
FIG. 26

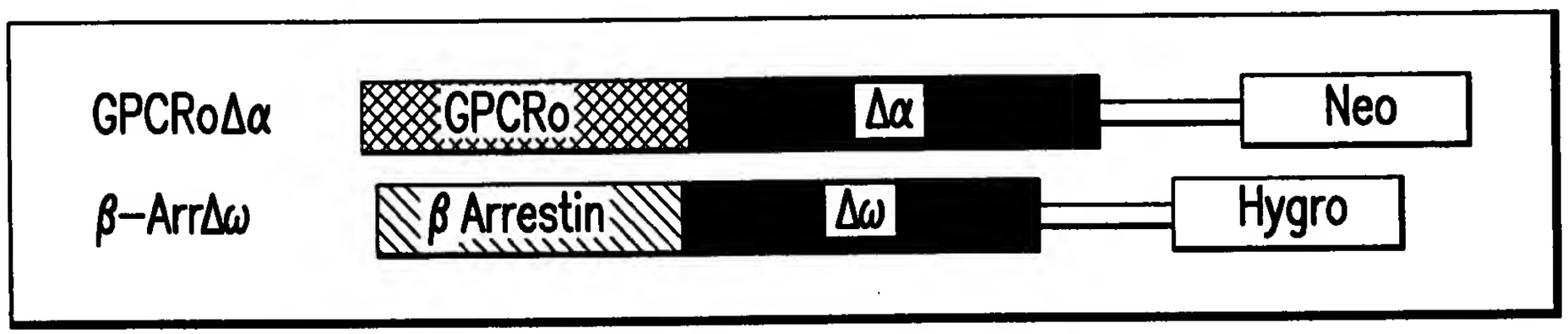


GPCR dimerization measured by β-gal complementation

FIG. 27

Example–





Ligand Fishing for Orphan Receptors by β–galactosidase mutant complementation in ICAST™ System

FIG. 28